

1	- - - - -	Hu p53
1	- - - - -	Hu p73 β
1	- - - - -	Hu p63 γ
1	M N F E T S R C A T L Q Y C P D P Y I Q R F I E T P A H F S W K E S I T R S A M	Mu p63 γ
4	P O S D P S V E P A I S Q E T T S D - - - - -	Hu p53
2	A G S T A T S - - D G G T T - - F E H I S S E E P D - - S T Y F - - - - - D	Hu p73 β
2	S S T Q T N E F - - S P H V - - F Q H I W D F I E Q P I C S V Q P I D L N F V D	Hu p63 γ
2	S S T Q T S E F - - S P H V - - F Q H I W D F I E Q P I C S V Q P I E L N F V D	Mu p63 γ
41	- - - - -	Hu p53
35	H I P - - - - -	Hu p53
31	A P O S S R G N N E V V G G T D S S - - M D V F H I E G - M T T S V M A Q F N L -	Hu p73 β
40	E P S E D G A T N K I E I S M D C I R M Q S D I S D P M W H Q Y T - - - N L G	Hu p63 γ
79	E P S E N G A T N K I E I S M D C I R M Q S D I S D P M W H Q Y T - - - N L G	Mu p63 γ
61	- - - - -	Hu p53
68	L S S T H D Q M - - - S S R A A S A S P Y - T P E H H A - S V E T - H S P Y A	Hu p73 β
77	L L N S M D Q Q I Q N G S S - - S T S P Y N T - D H Q Q N S V - T A A S P Y A	Hu p63 γ
116	L L N S M D Q Q I Q N G S S - - S T S P Y N T - D H Q Q N S V - T A A S P Y A	Mu p63 γ
90	- - - - -	Hu p53
101	C - - - - - T F D T M S P A P V I P S N D E P C P H H I E V T Q Q S S P A	Hu p73 β
112	Q - - - - - T F D A L S P S P A I P S N D D V P C P H S D D V S E Q Q S S P A	Hu p63 γ
151	C - - - - - T F D A L S P S P A I P S N D D V P C P H S D D V S E Q Q S S P A	Mu p63 γ
121	S W V I C T Y S P A I N K M I C O P Y X C E V O L W V D S I S C G T A	Hu p53
139	S A H T Y S H L K R L Y C O I A K T O P I I Q I K M S T P I P B C I A I	Hu p73 β
150	S A H T Y S H L K R L Y C O I A K T O P I I Q I K M M T P E P Q G A V I	Hu p63 γ
189	S A T W T Y S T E W K R L Y C O I A K T O P I I Q I K M M T P E P Q G A V I	Mu p63 γ
161	A T T N Q S S Y M T E A V R R Q P H E - - E G C S A S D G L A P P O H I T R V E	Hu p53
179	P V Y K K A E S V T E V W K R Q P N H E L S P E F N E G Q I A P S S H I T R V E	Hu p73 β
190	P V Y K K A E S V T E V W K R Q P N H E L S P E F N E G Q I A P S S H I T R V E	Hu p63 γ
229	P V Y K K A E S V T E V W K R Q P N H E L S P E F N E G Q I A P S S H I T R V E	Mu p63 γ
199	I G N I R V E V I D D R A T E P H S V V V E Y I P P E V G S D A T T T H Y N Y M C	Hu p53
219	G N N L S Q V V D D P V T G R C S V Y P P P Q V G T E F P I V L V N F M C	Hu p73 β
230	K N S H A Q Y V E D P I T G R C S V L A P Y P P P Q V G T E F P I V L V N F M C	Hu p63 γ
269	I G N S H A Q Y V E D P I T G R C S V L A P Y P P P Q V G T E F P I V L V N F M C	Mu p63 γ
239	N G S C V G G M N R R B I I I V I E D D S S G N I I G C N S I I I H V G A C P	Hu p53
259	N G S C V G G M N R R B I I I V I E D D S S G N I I G C N S I I I H V G A C P	Hu p73 β
270	N G S C V G G M N R R B I I I V I E D D S S G N I I G C N S I I I H V G A C P	Hu p63 γ
309	N G S C V G G M N R R B I I I V I E D D S S G N I I G C N S I I I H V G A C P	Mu p63 γ
279	G R D R K R T E E E N I R K G P R R H E P P C - - - - -	Hu p53
299	G R D R K A D E D P H Y R E Q Q A L N - E - - - - -	Hu p73 β
310	G R D R K A D E D S I R K Q Q V S - D - - - - -	Hu p63 γ
349	G R D R K A D E D S I R K Q Q V S - D - - - - -	Mu p63 γ
311	N - - - - -	Hu p53
333	- S P P A V P A L G A G V K I R R H G D E D T Y Y Q V E G T E N E E I L M K I	Hu p73 β
342	- T H G I Q M I S - - I K I R R S P D D E L L Y I P V E G T E T Y C M L L K I	Hu p63 γ
377	- T H G I Q M I S - - I K I R R S P D D E L L Y I P V E G T E T Y C M L L K I	Mu p63 γ
345	- - - - -	Hu p53
372	K E S I E P H E L V P Q P L V D S Y R Q Q Q Q - - - - -	Hu p73 β
379	K E S I E P H M Q Y L P Q H T I E T Y R Q Q Q Q Q Q H Q H L L Q K - - - - -	Hu p63 γ
414	K E S I E P H M Q Y L P Q H T I E T Y R Q Q Q Q Q Q H Q H L L Q K - - - - -	Mu p63 γ
372	- - - - -	Hu p53
407	Y G P V I L S P M N V H G G - - M N C I P S V N Q L V G O P P P H S S A A T P N	Hu p73 β
417	F R N E L V E P R R E T E P K Q S D - - V F F R H S K I P N R S V Y P Z	Hu p63 γ
452	F R N E L V E P R G E A P I Q S D - - V F F R H S N C P N H S V V Y P Z	Mu p63 γ
393	- - - - -	Hu p53
445	L G P V G P G M L N N H G A V P A N G E M S S S H S A Q S M V S G S H C T P P	Hu p73 β
448	- - - - -	Hu p63 γ
484	- - - - -	Mu p63 γ
393	P P Y H A D P S L V R T W G P	Hu p53
485	P P Y H A D P S L V R T W G P	Hu p73 β
448	- - - - -	Hu p63 γ
484	- - - - -	Mu p63 γ

FIGURE 1

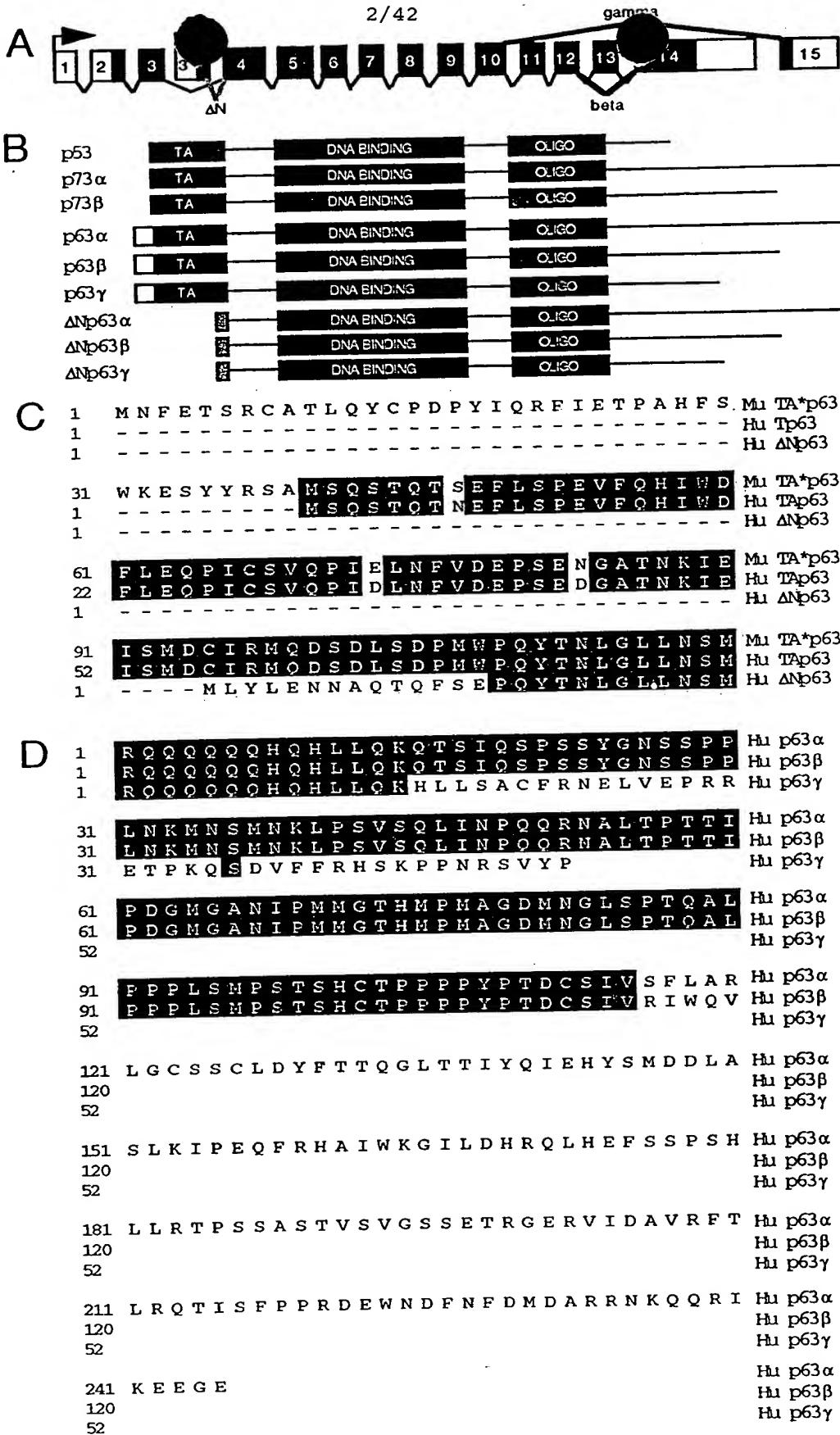


FIGURE 2

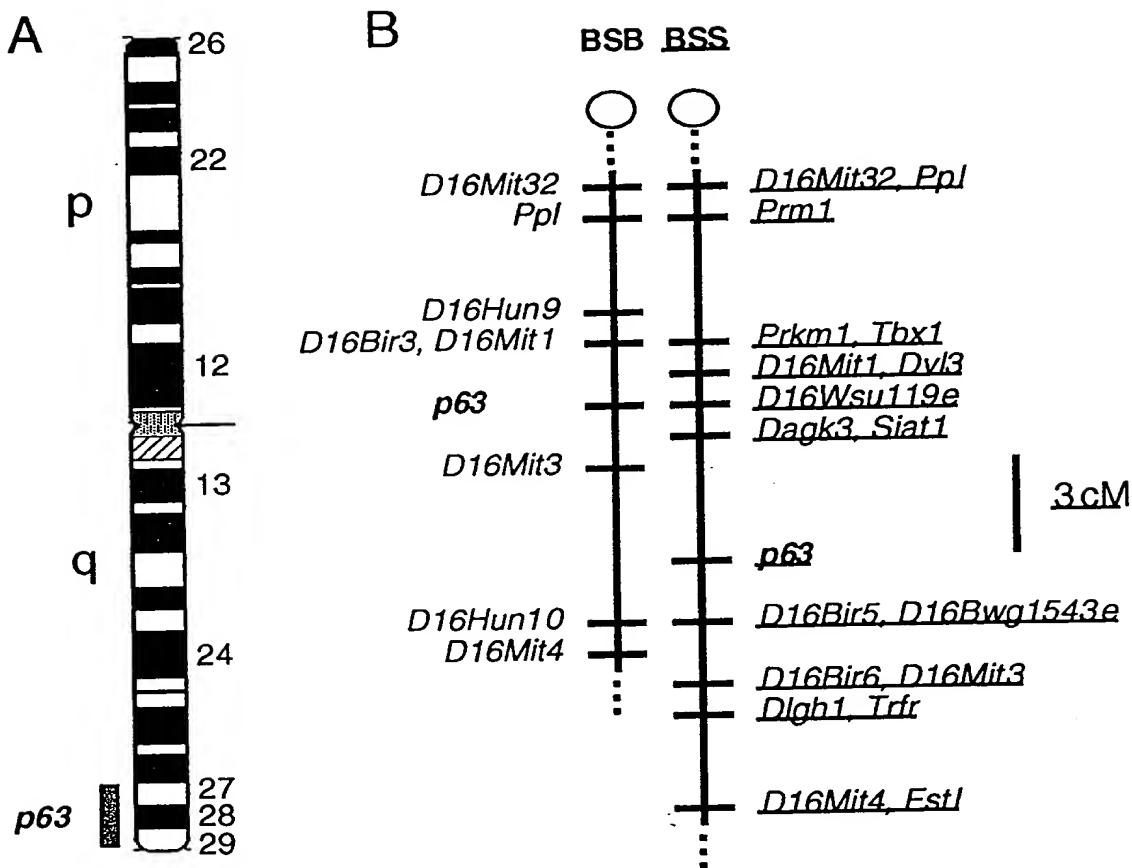


FIGURE 3

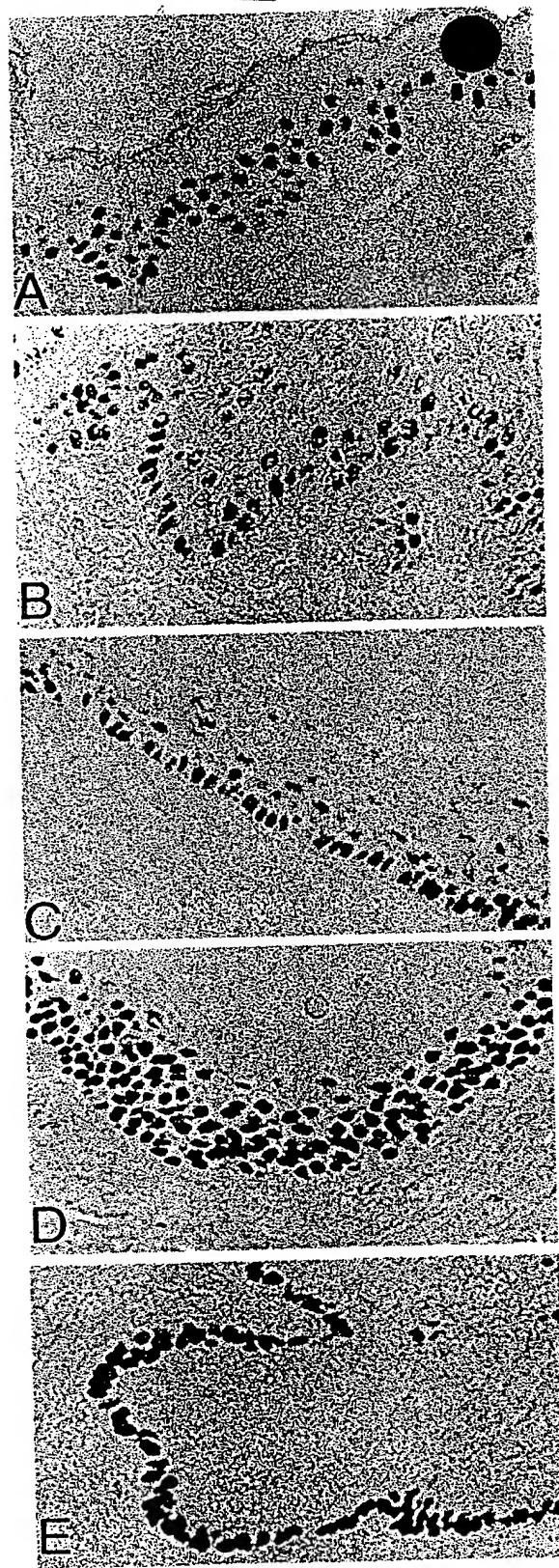


FIGURE 4

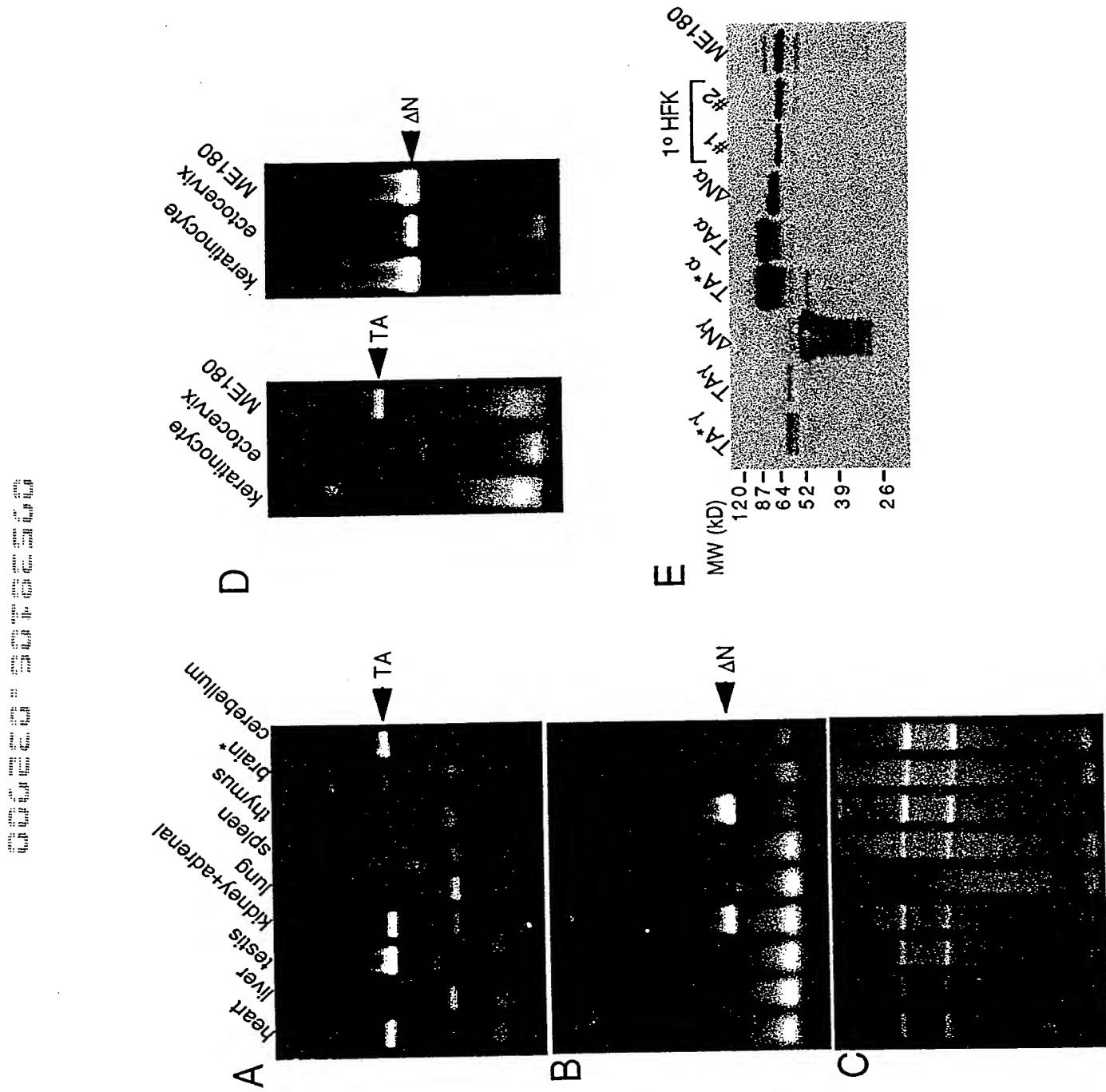


FIGURE 5

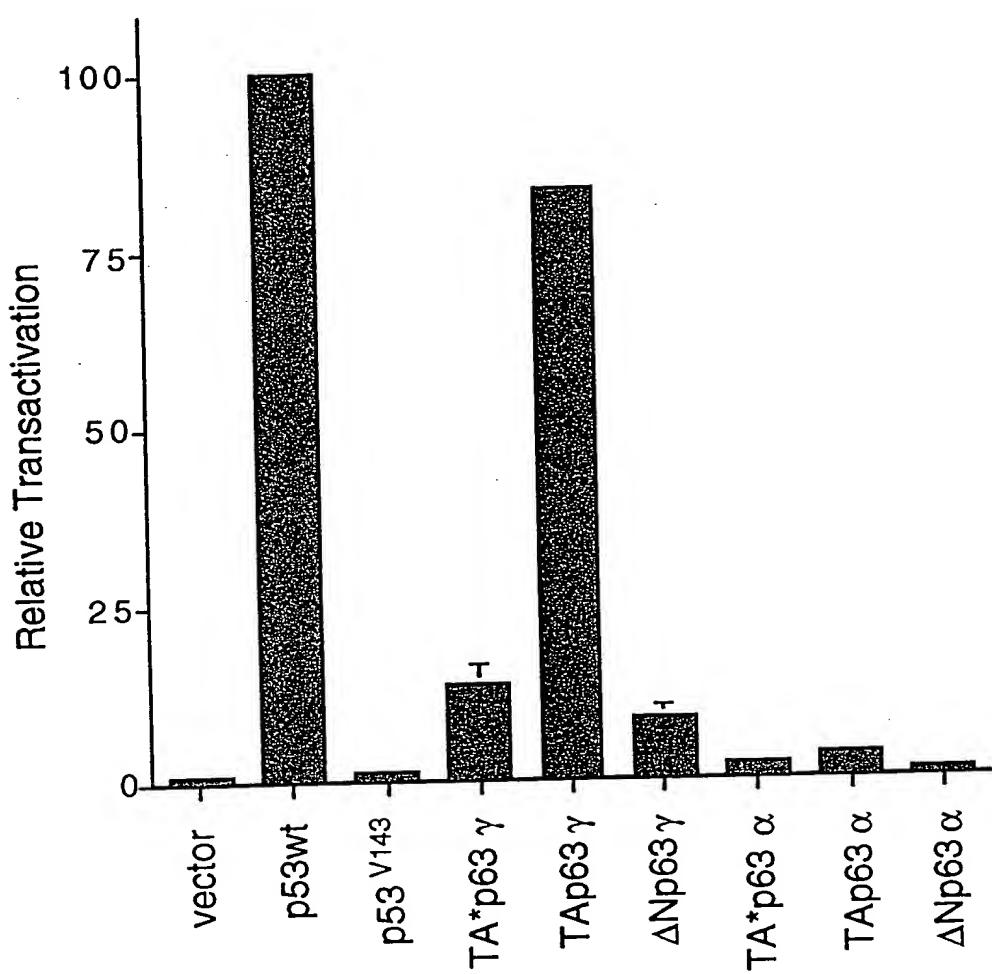


FIGURE 6

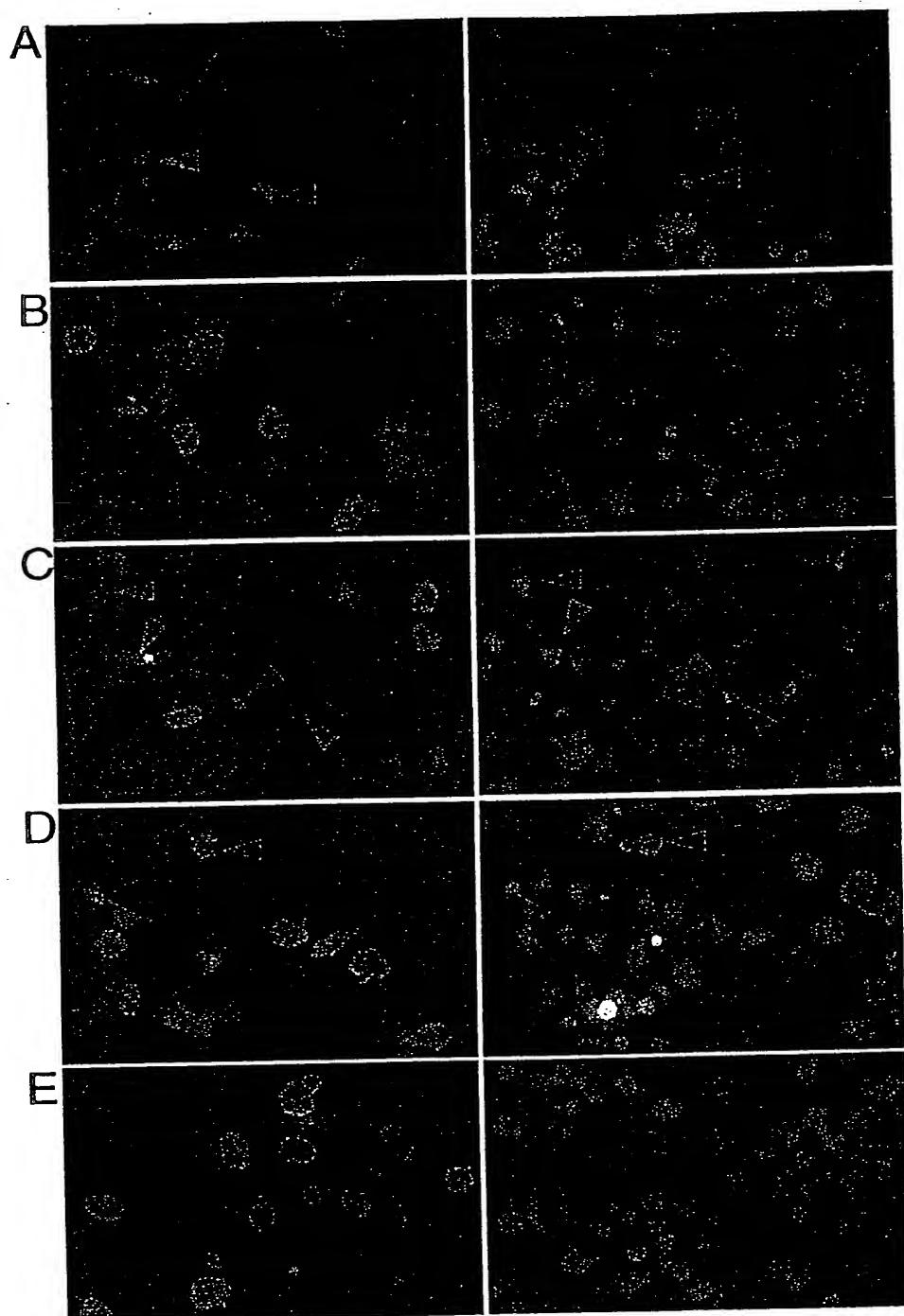


FIGURE 7

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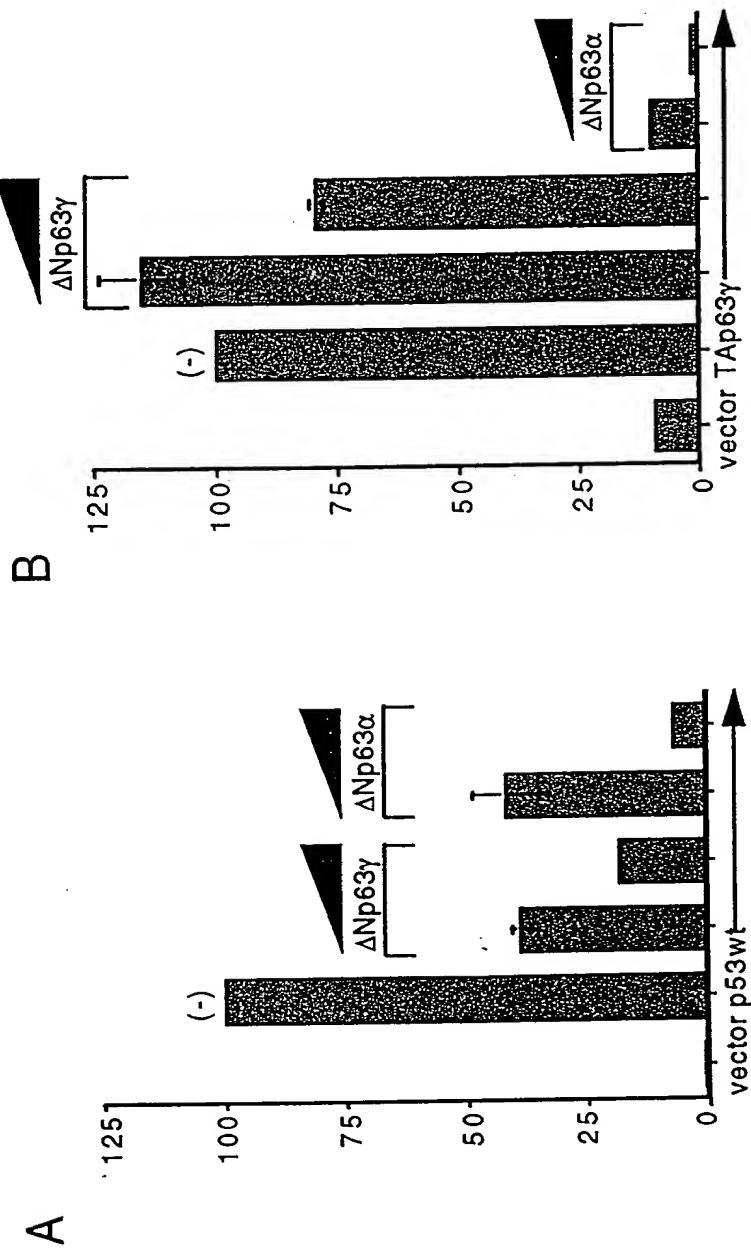


FIGURE 8

31/11

1/1 ATG TCC CAG AGC ACA CAG ACA AAT GAA TTC cTC AGT CCA GAG GTT TTC CAG CAT ATC TGG
M S Q S T Q T N E F L S P E V F Q H I W
61/21 91/31
GAT TTT CTG GAA CAG CCT ATA TGT TCA GTT CAG CCC ATT GAC TTG AAC TTT GTG GAT GAA
D F L E Q P I C S V Q P I D L N F V D E
121/41 151/51
CCA TCA GAA GAT GGT GCG ACA AAC AAG ATT GAG ATT AGC ATG GAC TGT ATC CGC ATG CAG
P S E D G A T N K I E I S M D C I R M Q
181/61 211/71
GAC TCG GAC CTG AGT GAC CCC ATG TGG CCA CAG TAC ACG AAC CTG GGG CTC CTG AAC AGC
D S D L S D P M W P Q Y T N L G L L N S
241/81 271/91
ATG GAC CAG CAG ATT CAG AAC GGC TCC TCG TCC ACC AGT CCC TAT AAC ACA GAC CAC GCG
M D Q Q I Q N G S S S T S P Y N T D H A
301/101 331/111
CAG AAC AGC GTC ACG GCG CCC TCG CCC TAC GCA CAG CCC AGC TCC ACC TTC GAT GCT CTC
Q N S V T A P S P Y A Q P S S T F D A L
361/121 391/131
TCT CCA TCA CCC GCC ATC CCC TCC AAC ACC GAC TAC CCA GGC CCG CAC AGT TTC GAC GTG
S P S P A I P S N T D Y P G P H S F D V
421/141 451/151
TCC TTC CAG CAG TCG AGC ACC GCC AAG TCG GCC ACC TGG ACG TAT TCC ACT GAA CTG AAG
S F Q Q S S T A K S A T W T Y S T E L K
481/161 511/171
AAA CTC TAC TGC CAA ATT GCA AAG ACA TGC CCC ATC CAG ATC AAG GTG ATG ACC CCA CCT
K L Y C Q I A K T C P I Q I X V M T P P
541/181 571/191
CCT CAG GGA GCT GTT ATC CGC GCC ATG CCT GTC TAC AAA AAA GCT GAG CAC GTC ACG GAG
P Q G A V I R A M P V Y K K A E H V T E
601/201 631/211
GTG GTG AAG CGG TGC CCC AAC CAT GAG CTG AGC CGT GAA TTC AAC GAG GGA CAG ATT GCC
V V K R C P N H E L S R E F N E G Q I A
661/221 691/231
CCT CCT AGT CAT TTG ATT CGA GTA GAG GGG AAC AGC CAT GCC CAG TAT GTA GAA GAT CCC
P P S H L I R V E G N S H A Q Y V E D P
721/241 751/251
ATC ACA CGA AGA CAG AGT GTG CTG GTA CCT TAT GAG CCA CCC CAG GTT GGC ACT GAA TTC
I T G R Q S V L V P Y E P P Q V G T E F
781/261 811/271
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T T V L Y N F M C N S S C V G G M N R R
841/281 871/291
CCA ATT TTA ATC ATT GTT ACT CTG GAA ACC AGA GAT GGG CAA GTC CTG GGC CGA CGC TGC
P I L I I V T L E T R D G Q V L G R R C
901/301 931/311
TTT GAG GCC CGG ATC TGT GCT TGC CCA GGA AGA GAC AGG AAG GCG GAT GAA GAT AGC ATC
F E A R I C A C P G R D R K A D E D S I
961/321 991/331
AGA AAG CAG CAA GTT TCG GAC AGT ACA AAG AAC GGT GAT GGT AGC AAG CGC CCG TTT CGT
R K Q Q V S D S T K N G D G T K R P F R
1021/341 1051/351
CAG AAC ACA CAT GGT ATC CAG ATG ACA TCC ATC AAG AAA CGA AGA TCC CCA GAT GAT GAA
Q N T H G I Q M T S I K K R R S P D D E
1081/361 1111/371
CTG TTA TAC TTA CCA GTG AGG GGC CGT GAG ACT TAT GAA ATG CTG TTG AAG ATC AAA GAG
L L Y L P V R G R E T Y E M L L K I K E
1141/381 1171/391
TCC CTG GAA CTC ATG CAG TAC CTT CCT CAG CAC ACA ATT GAA AGC TAC AGG CAA CAG CAA
S L E L M Q Y L P Q H T I E T Y R Q Q Q

1201/401 1231/411
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 Q Q Q H Q H L D Q K Q T S I Q S P S Y
 1261/421 1291/431
 GGT AAC AGC TCC CCA CCT CTG AAC AAA ATG AAC AGC ATG AAC AAG CTG CCT TCT GTG AGC
 G N S S P P L N K M N S M N K L P S V S
 1321/441 1351/451
 CAG CTT ATC AAC CCT CAG CAG CGC AAC GCC CTC ACT CCT ACA ACC ATT CCT GAT GGC ATG
 Q L I N P Q R N A L T P T T I P D G M
 1381/461 1411/471
 GGA GCC AAC ATT CCC ATG ATG GGC ACC CAC ATG CCA ATG GCT GGA GAC ATG AAT GGA CTC
 G A N I P M M G T H M P M A G D M N G L
 1441/481 1471/491
 AGC CCC ACC CAG GCA CTC CCT CCC CCA CTC TCC ATG CCA TCC ACC TCC CAC TGC ACA CCC
 S P T Q A L P P F L S M P S T S H C T P
 1501/501 1531/511
 CCA CCT CCG TAT CCC ACA GAT TGC AGC ATT GTC ACT TTC TTA GCG AGG TTG GGC TGT TCA
 P P P Y P T D C S I V S F L A R L G C S
 1561/521 1591/531
 TCA TGT CTG GAC TAT TTC ACG ACC CAG GGG CTG ACC ACC ATC TAT CAG ATT GAG CAT TAC
 S C L D Y F T T Q G L T T I Y Q I E H Y
 1621/541 1651/551
 TCC ATG GAT GAT CTG GCA AGT CTG AAA ATC CCT GAG CAA TTT CGA CAT GCG ATC TGG AAG
 S M D D L A S L K I P E Q F R H A I W K
 1681/561 1711/571
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 G I L D H R Q L H E F S S P S H L L R T
 1741/581 1771/591
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 D A V R F T L R Q T I S F P P R D E W N
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 GAC TTC AAC TTT GAC ATG GAT GCT CGC CGC AAT AAG CAA CAG CGC ATC AAA GAG GAG GGG
 D F N F D M D A R R N K Q Q R I K E E G
 1921/641
 GAG TGA
 E *

1/1 31/11
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 61/21 91/31
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 D F L E Q P I C S V Q P I D L N F V D E
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 181/61 211/71
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 241/81 271/91
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 301/101 331/111
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1201/401

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1381/461

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1231/411

1291/431

1351/451

1411/471

1471/491

1531/511

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 S F Q Q S S T A K S A T W T Y S T E L K
 481/161 511/171
 AAA CTC TAC TGC CAA ATT GCA AAG ACA TGC CCC ATC CAG ATC AAG GTG ATG ACC CCA CCT
 K L Y C Q I A X T C P I Q I K V M T P P
 541/181 571/191
 CCT CAG GGA GCT GTT ATC CGC GCC ATG CCT GTC TAC AAA AAA GCT GAG CAC GTC ACG GAG
 P Q G A V I R A M P V Y K K A E H V T E
 601/201 631/211
 GTG GTG AAG CGG TGC CCC AAC CAT GAG CTG AGC CGT GAA TTC AAC GAG GGA CAG ATT GCC
 V V K R C P N H E L S R E F N E G Q I A
 661/221 691/231
 CCT CCT AGT CAT TTG ATT CGA GTA GAG GGG AAC AGC CAT GCC CAG TAT GTA GAA GAT CCC
 P P S H L I R V E G N S H A Q Y V E D P
 721/241 751/251
 ATC ACA GGA AGA CAG AGT GTG CTG GTA CCT TAT GAG CCA CCC CAG GTT GGC ACT GAA TTC
 I T G R Q S V L V P Y E P P Q V G T E F
 781/261 811/271
 ACG ACA GTC TTG TAC AAT TTC ATG TGT AAC AGC AGT TGT GTT GGA CGG ATG AAC CGC CGT
 T T V L Y N F M C N S S C V G G M N R R
 841/281 871/291
 CCA aTT TTA ATC ATT GTT ACT CTG GAA ACC AGA GAT GGG CAA GTC CTG GGC CGA CGC TGC
 P I L I I V T L E T R D G Q V L G R R C
 901/301 931/311
 TTT GAG GCC CGG ATC TGT GCT TGC CCA GGA AGA GAC AGG AAG GCG GAT GAA GAT AGC ATC
 F E A R I C A C P G R D R K A D E D S I
 961/321 991/331
 AGA AAG CAG CAA GTT TCG GAC AGT ACA AAG AAC GGT GAT GGT ACG AAG CGC CGG TTT CGT
 R K Q Q V S D S T K N G D G T K R P F R
 1021/341 1051/351
 CAG AAC ACA CAT GGT ATC CAG ATG ACA TCC ATC AAG AAA CGA AGA TCC CCA GAT GAT GAA
 Q N T H G I Q M T S I K K R R S P D D E
 1081/361 1111/371
 CTG TTA TAC TTA CCA GTG AGG GGC CGT GAG ACT TAT GAA ATG CTG TTG AAG ATC AAA GAG
 L L Y L P V R G R E T Y E M L L K I K E
 1141/381 1171/391
 TCC CTG GAA CTC ATG CAG TAC CTT CCT CAG CAC ACA ATT GAA ACG TAC AGG CAA CAG CAA
 S L E L M Q Y L P Q H T I E T Y R Q Q Q

14/42

1201/401

CAG CAG CAG CAC CAG CAC T T CAG AAA CAT CTC CTT TCA GCC TGC T G G AAT GAG
Q Q H Q L L Q K H L L S A C F R N E
1261/421 1291/431
CTT CTG GAG CCC CGG AGA GAA ACT CCA AAA CAA TCT GAC GTC TTC TTT AGA CAT TCC AAG
L V E P R R E T P K Q S D V F F R H S K
1321/441
CCC CCA AAC CGA TCA GTG TAC CCA TAG
P P N R S V Y P *

DNA sequence analysis of the 5' flanking region of the human gene for the 5'-nucleotidase

FIGURE 11 (CONT'D)

1/1 31/11
ATG TTG TAC CTG GAA AAC AAT GCC CAG ACT CAA TTT AGT GAG CCA CAG TAC ACG AAC CTG
M L Y L E N N A Q T Q F S E P Q Y T N L
61/21 91/31
GGG CTC CTG AAC AGC ATG GAC CAG CAG ATT CAG AAC GGC TCC TCG TCC ACC AGT CCC TAT
G L L N S M D Q Q I Q N G S S S T S P Y
121/41 151/51
AAC ACA GAC CAC GCG CAG AAC AGC GTC ACG GCG CCC TCG CCC TAC GCA CAG CCC AGC TCC
N T D H A Q N S V T A P S P Y A Q P S S
181/61 211/71
ACC TTC GAT GCT CTC TCT CCA TCA CCC GCC ATC CCC TCC AAC ACC GAC TAC CCA GGC CGC
T F D A L S P S P A I P S N T D Y P G P
241/81 271/91
CAC AGT TTC GAC GTG TCC TTC CAG CAG TCG AGC ACC GCC AAG TCG GCC ACC TGG ACG TAT
H S F D V S F Q Q S S T A K S A T W T Y
301/101 331/111
TCC ACT GAA CTG AAG AAA CTC TAC TGC CAA ATT GCA AAG ACA TGC CCC ATC CAG ATC AAG
S T E L K K L Y C Q I A K T C P I Q I K
361/121 391/131
GTG ATG ACC CCA CCT CCT CAG GGA GCT GTT ATC CGC GCC ATG CCT GTC TAC AAA AAA GCT
V M T P P P Q G A V I R A M P V Y K K A
421/141 451/151
GAG CAC GTC ACG GAG GTG GTG AAG CGG TGC CCC AAC CAT GAG CTG AGC CGT GAA TTC AAC
E H V T E V V K R C P N H E L S R E F N
481/161 511/171
GAG GGA CAG ATT GCC CCT CCT AGT CAT TTG ATT CGA GTA GAG GGG AAC AGC CAT GCC CAG
E G Q I A P P S H L I R V E G N S H A Q
541/181 571/191
TAT GTA GAA GAT CCC ATC ACA GGA AGA CAG AGT GTG CTG GTA CCT TAT GAG CCA CCC CAG
Y V E D P I T G R Q S V L V P Y E P P Q
601/201 631/211
GTT GGC ACT GAA TTC ACG ACA GTC TTG TAC ATT TTC ATG TGT AAC ACC AGT TGT GTT GGA
V G T E F T T V L Y N F M C N S S C V G
661/221 691/231
GGG ATG AAC CgC Cgt CCa aTT TTA ATC ATT GTT ACT CTG GAA ACC AGA GAT GGG CAA GTC
G M N R R P I L I I V T L E T R D G Q V
721/241 751/251
CTG GGC CGA CGC TGC TTT GAG GCC CCG ATC TGT GCT TGC CCA GGA AGA GAC AGG AAG GCG
L G R R C F E A R I C A C P G R D R K A
781/261 811/271
GAT GAA GAT AGC ATC AGA AAG CAG CAA GTT TCG GAC AGT ACA AAG AAC GGT GAT GGT ACG
D E D S I R K Q Q V S D S T K N G D G T
841/281 871/291
AAG CGC CCG TTT CGT CAG AAC ACA CAT GGT ATC CAG ATG ACA TCC ATC AAG AAA CGA AGA
K R P F R Q N T H G I Q M T S I K K R R
901/301 931/311
TCC CCA GAT GAT GAA CTG TTA TAC TTA CCA GTG AGG GGC CGT GAG ACT TAT GAA ATG CTG
S P D D E L L Y L P V R G R E T Y E M L
961/321 991/331
TTG AAG ATC AAA GAG TCC CTG GAA CTC ATG CAG TAC CTT CCT CAG CAC ACA ATT GAA ACG
L K I K E S L E L M Q Y L P Q H T I E T
1021/341 1051/351
TAC AGG CAA CAG CAA CAG CAG CAG CAC CAG CAC TTA CTT CAG AAA CAG ACC TCA ATA CAG
Y R Q Q Q Q Q H Q H L L Q K Q T S I Q
1081/361 1111/371
TCT CCA TCT TCA TAT GGT AAC AGC TCC CCA CCT CTG AAC AAA ATG AAC AGC ATG AAC AAG
S P S S Y G N S S P P L N K M N S M N K
1141/381 1171/391
CTG CCT TCT GTG AGC CAG CTT ATC AAC CCT CAG CAG CGC AAC GCC CTC ACT CCT ACA ACC
L P S V S Q L I N P Q Q R N A L T P T T

1201/401

ATT CCT GAT GGC ATG GGA GCC AAC ATT CCC ATG ATG GGC ACC CAC ATG CCA ATG GCT GGA
 I P D G M G A N I P M M G T H M P M A G

1261/421

GAC ATG AAT GGA CTC AGC CCC ACC CAG GCA CTC CCT CCC CCA CTC TCC ATG CCA TCC ACC
 D M N G L S P T Q A L P P L S M P S T

1321/441

TCC CAC TGC ACA CCC CCA CCT CCG TAT CCC ACA GAT TGC AGC ATT GTC ACT TTC TTA GCG
 S H C T P P P X P T D C S I V S F L A

1381/461

1351/451
 AGG TTG GGC TGT TCA TCA TGT CTG GAC TAT TTC ACG ACC CAG GGG CTG ACC ACC ATC TAT
 R L G C S S C L D Y F T T Q G L T T I Y

1441/481

1471/491
 CAG ATT GAG CAT TAC TCC ATG GAT GAT CTG GCA AGT CTG AAA ATC CCT GAG CAA TTT CGA
 Q I B H Y S M D D L A S L K I P E Q F R

1501/501

1531/511
 CAT CGG ATC TGG AAG GGC ATC CTG GAC CAC CGG CAG CTC CAC GAA TTC TCC TCC CCT TCT
 H A I W K G I L D H R Q L H E F S S P S

1561/521

1591/531
 CAT CTC CTG CGG ACC CCA AGC AGT GCC TCT ACA GTC AGT GTG GGC TCC AGT GAG ACC CGG
 H L L R T P S S A S T V S V G S S E T R

1621/541

1651/551
 GGT GAG CGT GTT ATT GAT GCT GTG CGA TTC ACC CTC CGC CAG ACC ATC TCT TTC CCA CCC
 G E R V I D A V R F T L R Q T I S F P P

1681/561

1711/571
 CGA GAT GAG TGG AAT GAC TTC AAC TTT GAC ATG GAT GCT CGC CGC AAT AAG CAA CAG CGC
 R D E W N D F N F D M D A R R N K Q Q R

1741/581

ATC AAA GAG GAG GGG GAG TGA
 I K E E G E *

FIGURE 12 (CONT'D)

1/1 31/11
ATG TTG TAC CTG GAA AAC AAT GCC CAG ACT CCA TTT AGT GAG CCA CAG TAC ACG AAC CTG
M L Y L E N N A Q T Q F S E P Q Y T N L
61/21 91/31
GGG CTC CTG AAC AGC ATG GAC CAG CAG ATT CAG AAC GGC TCC TCG TCC ACC ACT CCC TAT
G L L N S M D Q Q I Q N G S S S T S P Y
121/41 151/51
AAC ACA GAC CAC GCG CAG AAC AGC GTC ACG GCG CCC TCG CCC TAC GCA CAG CCC AGC TCC
N T D H A Q N S V T A P S P Y A Q P S S
181/61 211/71
ACC TTC GAT GCT CTC TCT CCA TCA CCC GCC ATC CCC TCC AAC ACC GAC TAC CCA GGC CCG
T F D A L S P S P A I P S N T D Y P G P
241/81 271/91
CAC AGT TTC GAC GTG TCC TTC CAG CAG TCG AGC ACC GCC AAG TCG GCC ACC TGG ACG TAT
H S F D V S F Q Q S S T A K S A T W T Y
301/101 331/111
TCC ACT GAA CTG AAG AAA CTC TAC TGC CAA ATT GCA AAG ACA TGC CCC ATC CAG ATC AAG
S T E L K K L Y C Q I A K T C P I Q I X
361/121 391/131
GTG ATG ACC CCA CCT CCT CAG GGA GCT GTT ATC CGC GCC ATG CCT GTC TAC AAA AAA GCT
V M T P P P Q G A V I R A M P V Y K K A
421/141 451/151
GAG CAC GTC ACG GAG GTG GTG AAG CGG TGC CCC AAC CAT GAG CTG AGC CGT GAA TTC AAC
E H V T E V V K R C P N H E L S R E F N
481/161 511/171
GAG GGA CAG ATT GCC CCT CCT AGT CAT TTG ATT CGA GTA GAG GGG AAC AGC CAT GCC CAG
E G Q I A P P S H L I R V E G N S H A Q
541/181 571/191
TAT GTA GAA GAT CCC ATC ACA GGA AGA CAG AGT GTG CTG GTA CCT TAT GAG CCA CCC CAG
Y V E D P I T G R Q S V L V P Y E P P Q
601/201 631/211
GTT GGC ACT GAA TTC ACG ACA GTC TTG TAC AAT TTC ATG TGT AAC AGC AGT TGT GTT GGA
V G T E F T T V L Y N F M C N S S C V G
661/221 691/231
GGG ATG AAC cgC Cgt CCA aTT TTA ATC ATT GTT ACT CTG GAA ACC AGA GAT GGG CAA GTC
G M N R R P I L I I V T L E T R D G Q V
721/241 751/251
CTG GGC CGA CGC TGC TTT GAG GCC CGG ATC TGT GCT TGC CCA GGA AGA GAC AGG AAG GCG
L G R R C F E A R I C A C P G R D R K A
781/261 811/271
GAT GAA GAT AGC ATC AGA AAG CAG CAA GTT TCG GAC AGT ACA AAG AAC GGT GAT GGT ACG
D E D S I R K Q Q V S D S T K N G D G T
841/281 871/291
AAG CGC CCG TTT CGT CAG AAC ACA CAT GGT ATC CAG ATG ACA TCC ATC AAG AAA CGA AGA
K R P F R Q N T H G I Q M T S I X K R R
901/301 931/311
TCC CCA GAT GAT GAA CTG TTA TAC TTA CCA GTG AGG GGC CGT GAG ACT TAT GAA ATG CTG
S P D D E L L Y L P V R G R E T Y E M L
961/321 991/331
TTG AAG ATC AAA GAG TCC CTG GAA CTC ATG CAG TAC CTT CCT CAG CAC ACA ATT GAA ACG
L K I K E S L E L M Q Y L P Q H T I E T
1021/341 1051/351
TAC AGG CAA CAG CAA CAG CAG CAC CAG CAC TTA CTT CAG AAA CAG ACC TCA ATA CAG
Y R Q Q Q Q Q Q H Q H L L Q K Q T S I Q
1081/361 1111/371
TCT CCA TCT TCA TAT GGT AAC AGC TCC CCA CCT CTG AAC AAA ATG AAC AGC ATG AAC AAG
S P S S Y G N S S P P L N K M N S M N K
1141/381 1171/391
CTG CCT TCT GTG AGC CAG CTT ATC AAC CCT CAG CAG CGC AAC GCC CTC ACT CCT ACA ACC
L P S V S Q L I N P Q Q R N A L T P T T

18/42

1201/401 1231/411
 ATT CCT GAT GGC ATG G [REDACTED] CC AAC ATT CCC ATG ATG GGC ACC CAC A [REDACTED] CA ATG GCT GGA
 I P D G M C A N I P M M G T H M P M A G
 1261/421 1291/431
 GAC ATG AAT GGA CTC ASC CCC ACC CAG GCA CTC CCT CCC CCA CTC TCC ATG CCA TCC ACC
 D M N G L S P T Q A L P P P L S M P S T
 1321/441 1351/451
 TCC CAC TGC ACA CCC CCA CCT CGG TAT CCC ACA GAT TGC AGC ATT GTC AGG ATC TGG CAA
 S K C T P F P P Y P T D C S I V R I W Q
 1381/461
 GTC TGA
 V "

FIGURE 13A (CONT'D)

1/1 31/11
ATG TTG TAC CTG GAA AAC AAT GCC CAG ACT CAA TTT AGT GAG CCA CAG TAC ACG AAC CTG
M L Y L E N N A Q T Q F S E P Q Y T N L
61/21 91/31
GGG CTC CTG AAC AGC ATG GAC CAG CAG ATT CAG AAC GGC TCC TCG TCC ACC AGT CCC TAT
G L L N S M D Q Q I Q N G S S S T S P Y
121/41 151/51
AAC ACA GAC CAC GCG CAG AAC AGC GTC ACG GCG CCC TCG CCC TAC GCA CAG CCC AGC TCC
N T D H A Q N S V T A P S P Y A Q P S S
181/61 211/71
ACC TTC GAT GCT CTC TCT CCA TCA CCC GCC ATC CCC TCC AAC ACC GAC TAC CCA GGC CCG
T F D A L S P S P A I P S N T D Y P G P
241/81 271/91
CAC AGT TTC GAC GTG TCC TTC CAG CAG TCG AGC ACC GCC AAG TCG GCC ACC TGG ACG TAT
H S F D V S F Q Q S S T A K S A T W T Y
301/101 331/111
TCC ACT GAA CTG AAG AAA CTC TAC TGC CAA ATT GCA AAG ACA TGC CCC ATC CAG ATC AAG
S T E L K K L Y C Q I A K T C P I Q I K
361/121 391/131
GTG ATG ACC CCA CCT CCT CAG GGA GCT GTT ATC CGC GCC ATG CCT GTC TAC AAA AAA GCT
V M T P P P Q G A V I R A M P V Y K K A
421/141 451/151
GAG CAC GTC ACG GAG GTG GTG AAG CGG TGC CCC AAC CAT GAG CTG AGC CGT GAA TTC AAC
E H V T E V V K R C P N H E L S R E F N
481/161 511/171
GAG CGA CAG ATT GCC CCT CCT AGT CAT TTG ATT CGA GTC GAG GGG AAC AGC CAT GCC CAG
E G Q I A P P S H L I R V E G N S K A Q
541/191 571/191
TAT GTA GAA GAT CCC ATC ACA GGA AGA CAG AGT GTG CTG GTA CCT TAT GAG CCA CCC CAG
Y V E D P I T G R Q S V L V P Y E P P Q
601/201 631/211
GTT GGC ACT GAA TTC ACG ACA GTC TTG TAC AAT TTC ATG TGT AAC AGC AGT TGT GTT GGA
V G T E F T T V L Y N F M C N S S C V G
661/221 691/231
GGG ATG AAC CGC Cgt CCA aTT TTA ATC ATT GTT ACT CTG GAA ACC AGA GAT GGG CAA GTC
G M N R R P I L I I V T L E T R D G Q V
721/241 751/251
CTG GGC CGA CGC TGC TTT GAG GCC CGG ATC TGT GCT TGC CCA GGA AGA GAC AGG AAG GCG
L G R R C F E A R I C A C P G R D R K A
781/261 811/271
CAT GAA GAT AGC ATC AGA AAG CAG CAA GTT TCG GAC AGT ACA AAG AAC GGT GAT GGT ACG
D E D S I R K Q Q V S D S T K N G D G T
841/281 871/291
AAG CGC CCG TTT CGT CAG AAC ACA CAT GGT ATC CAG ATG ACA TCC ATC AAG AAA CGA AGA
K R P F R Q N T H G I Q M T S I K K R R
901/301 931/311
TCC CCA GAT GAT GAA CTC TTA TAC TTA CCA GTG AGG GGC CGT GAG ACT TAT GAA ATG CTG
S P D D E L L Y L P V R G R E T Y E M L
961/321 991/331
TTG AAG ATC AAA GAG TCC CTG GAA CTC ATG CAG TAC CTT CCT CAG CAC ACA ATT GAA ACG
L K I K E S L E L M Q Y L P Q H T I E T
1021/341 1051/351
TAC AGG CAA CAG CAA CAG CAG CAC CAG CAC TTA CTT CAG AAA CAT CTC CTT TCA GCC
Y R Q Q Q Q Q Q H Q H L L Q K H L L S A
1081/361 1111/371
TGC TTC AGG AAT GAG CTT GTG GAG CCC CGG AGA GAA ACT CCA AAA CAA TCT GAC GTC TTC
C F R N E L V E P R R E T P K Q S D V F
1141/381 1171/391
TTT AGA CAT TCC AAG CCC CCA AAC CGA TCA GTG TAC CCA TAG
F R H S K P P N R S V Y P *

1/1 31/11
ATG AAT TTT GAA ACT TCA CGG TGT GCC ACC CTA CAG TAC TGC CCC GAC CCT TAC ATC CAG
M N F E T S R C A T L Q Y C P D P Y I Q
61/21 91/31
CGT TTC ATA GAA ACC CCA GCT CAT TTC TCG TGG AAA GAA AGT TAT TAC AGA TCT GCC ATG
R F I E T P A H F S W K E S Y Y R S A M
121/41 151/51
TCG CAG ACC ACC CAG ACA AGC GAG TTC CTC AGC CCA GAG GTC TTC CAG CAT ATC TGG GAT
S Q S T Q T S B F L S P E V F Q H I W D
181/61 211/71
TTT CTG GAA CAG CCT ATA TGC TCA GTA CAG ccc ATC GAG TTG AAC TTT GTG GAT GAA CCT
F L E Q P I C S V Q P I E L N F V D E P
241/81 271/91
TCC GAA AAT GGT GCa aCa aaC aag ATT GAG ATT AGC ATG GAT TGT Atc CGC ATG Caa GAc
S E N G A T N K I E I S M D C I R M Q D
301/101 331/111
TCA GAC cTC AGT GAc ccc ATG Tgg CCA CAG TAC ACG AAC CTG GGG CTC CTG AAC AGC ATG
S D L S D P M W P Q Y T N L G L L N S M
361/121 391/131
GAC CAG CAG ATT CAG AAC GGC TCC TCG TCC ACC AGC CCC TAC Aac ACA GAC CAC GCA CAG
D Q Q I Q N G S S S T S P Y N T D H A Q
421/141 451/151
TAT AGC GTG ACG GCG CCC TCG CCC TAT GCA CAG CCC AGC TCC ACC TTT GAT GCC CTC TCT
N S V T A P S P Y A Q P S S T F D A L S
481/161 511/171
CCA TCC CCT GCC ATT CCC TCC AAC ACA GAT TAC CCG GCC CCA CAC AGC TTC GAT GTG TCC
P S P A I P S N T D Y P G P H S F D V S
541/181 571/191
TTC CAG CAG TCA AGC ACT GCC AAG TCA GCC ACC TGG ACG TAT TCC ACC GAA CTG AAG AAG
F Q Q S S T A K S A T W T Y S T E L K K
601/201 631/211
CTG TAC TGC CAG ATT GCG AAG ACA TGC CCC ATC CAG ATC AAG GTG ATG ACC CCA CCC CCA
L Y C Q I A K T C P I Q I K V M T P P P
661/221 691/231
CAG GGC GCT GTt ATC CGT GCC ATG CCT GTC TAC AAG AAA GCT GAG CAT CTC ACC GAG GTT
Q G A V I R A M P V Y K K A E H V T E V
721/241 751/251
GTG AAA CGA TGC CCT AAC CAT GAG CTG AGC CGT GAG TTC AAT GAG GGA CAG ATT GCC CCT
V K R C P N H E L S R E F N E G Q I A P
781/261 811/271
CCC AGT CAT CTG ATT CGA GTA gAA GGG AAC AGC CAT GCC CAG TAT GTA GAA GAT CCT ATC
P S H L I R V E G N S H A Q Y V E D P I
841/281 871/291
ACG GGA AGG CAG AGC GTG CTG GTC CCT TAT GAG CCA CCA CaG GTT GGC ACT GAA TTC ACA
T G R Q S V L V P Y E P F Q V G T E F T
901/301 931/311
ACA GTC CTG TAC aAT TTC ATG TGT AAC AGC AGC TGC GTC GGA GGA ATG AAC AGA CGT CCA
T V L Y N F M C N S S C V G G M N R R P
961/321 991/331
ATT TTA ATC ATC GTT ACT CTG GAA ACC AGA GAT GGG CAA GTC CTG GGC CGA CGG TGC TTT
I L I I V T L E T R D G Q V L G R R C F
1021/341 1051/351
GAG GCC CGG ATC TGT Gct TGC CCA GGA AGA GAC CGG AAG GCA GAT GAA GAC AGC ATC AGA
E A R I C A C P G R D R K A D E D S I R
1081/361 1111/371
AAG CAG CAA GTA TCG GAC AGC GCA AAG AAC GGC GAT GGT ACG AAG CGC CCT TTC CGT CAG
K Q Q V S D S A K N G D G T K R P F R Q
1141/381 1171/391
AAT ACA CAC GGA ATC CAG ATG ACT TCC ATC AAG AAA CGG AGA TCC CCA GAT GAT GAG CTG
N T H G I Q M T S I K K R R S P D D E L

1201/401	1231/411
CTG TAC CTA CCA GTG AGA GGT	GAG ACG TAC GAG ATG TTG CTG AAG ATG A GAG TCA
L Y L P V R G R E T	Y E M L L K I K E S
1261/421	1291/431
CTG GAG CTC ATG CAG TAC CTC CCT CAG CAC	ACG ATC GAA ACG TAC ACC CAG CAG CAG CAG CAG
L E L M Q Y L P Q H	T I E T Y R Q Q Q Q
1321/441	1351/451
CAG CAG CAC CAG CAC CTA CTT CAG AAA CAG	ACC TCG ATG CAG TCT CAG TCT TCA TAT GGC
Q Q H Q H L L Q K Q	T S M Q S Q S S Y G
1381/461	1411/471
AAC AGT TCC CCA CCT CTG AAC AAA ATG AAC	AGC ATG AAC AAG CTG CCT TCC GTG AGC CAG
N S S P P L N K M N	S M N K L P S V S Q
1441/481	1471/491
CTT ATC AAC CCA CAG CAG CGC AAT GCC CTC	ACT CCC ACC ACC ATG CCT GAG GGC ATG GGA
L I N P Q Q R N A L	T P T T M P E G M G
1501/501	1531/511
GCC AAC ATT CCT ATG ATG GGC ACT CAC ATG	CCA ATG GCT GGA GAC ATG AAT GGA CTC AGC
A N I P M M G T H M	P M A G D M N G L S
1561/521	1591/531
CCT ACC CAA GCT CTC CCT CCA CTC TCC	ATG CCC TCC ACC TCC CAC TGC ACC CCA CCA
P T Q A L P P L S	M P S T S H C T P P
1621/541	1651/551
CCG CCC TAC CCC ACA GAC TGC AGC ATT GTC	AGT TTC TTA GCA Agg Ttg ggC TGC TCA TCA
F P Y P T D C S I V	S F L A R L G C S S
1681/561	1711/571
TGC CTG GAC TAT TTC ACC ACC CAG ggg CTG	Acc ACC ATC TaT CAG ATT GAG CAT TAC TCC
C L D Y F T T Q G L	T T I Y Q I E H Y S
1741/581	1771/591
ATG GAT GAT TCG GCa aGT CTG AAG ATc ccT	GAA CAG TTC CGA CAT GCC ATC TGG AAg GGC
M D D L A S L K I P	E Q F R H A I W K G
1801/601	1831/611
aTC CTG GAc CAC AGG cAG cTG CAC GAC TTC	TCC TCA CCT CCT Cat CTC CTG AGG ACC CCA
I L D H R Q L H D F	S S P P H L L R T P
1861/621	1891/631
AGT GGT GCC TCT ACC GTC AGT GTG GGC TCC	AGT GAG ACC CGT GGT GAA CGT GTG ATC GAT
S G A S T V S V G S	S E T R G E R V I D
1921/641	1951/651
GCC GTG CGC TTT ACC CTC CGC CAG ACC ATC	TCT TTT CCA CCC CGT GAC GAG TGG AAT GAT
A V R F T L R Q T I	S F P P R D E W N D
1981/661	2011/671
TTC AAC TTT GAC ATG GAT TCT CGT CGC AAC	AAG CAG CAG CGT ATC AAA GAG GAA GGA GAA
F N F D M D S R R N K	Q Q R I K E E G E
2041/681	
TGA	
*	

FIGURE 15 (CONT'D)

1/1 31/11
 ATG AAT TTT GAA ACT TCA CGG TGT GCC ACC CTA CAG TGC CCC GAC CCT TAC ATC CAG
 M N F E T S R C A T L Q Y C P D P Y I Q
 61/21 91/31
 CGT TTC ATA GAA ACC CCA GCT CAT TTC TCG TGG AAA GAA AGT TAT TAC AGA TCT GCC ATG
 R F I E T P A H F S W K E S Y Y R S A M
 121/41 151/51
 TCG CAG AGC ACC CAG ACA AGC GAG TTC CTC AGC CCA GAG GTC TTC CAG CAT ATC TGG GAT
 S Q S T Q T S E F L S P E V F Q H I W D
 181/61 211/71
 TTT CTG GAA CAG CCT ATA TGC TCA GTA CAG ccc ATC GAG TTG AAC TTT GTG GAT GAA CCT
 F L E Q P I C S V Q P I E L N F V D E P
 241/81 271/91
 TCC GAA AAT GGT CCa &Ca aaC aaG ATT GAG ATT AGC ATG GAT TGT ATc cGC ATG Caa GAc
 S E N G A T N K I E I S M D C I R M Q D
 301/101 331/111
 TCA GAC CTC AGT GAc ccc ATG Tgg CCA CAG TAC ACG AAC CTG GGG CTC CTG AAC AGC ATG
 S D L S D P M W P Q Y T N L G L L N S M
 361/121 391/131
 GAC CAG CAG ATT CAG AAC GGC TCC TCG TCC ACC AGC CCC TAC AaC ACA GAC CAC GCA CAG
 D Q Q I Q N G S S S T S P Y N T D H A Q
 421/141 451/151
 AAT AGC GTG ACG GCG CCC TCG CCC TAT GCA CAG CCC AGC TCC ACC TTT GAT GCC CTC TCT
 N S V T A P S P Y A Q P S S T F D A L S
 481/161 511/171
 CCA TCC CCT GCC ATT CCC TCC AAC ACA GAT TAC CCG GGC CCA CAC AGC TTC GAT GTG TCC
 P S P A I P S N T D Y P G P H S F D V S
 541/181 571/191
 TTC CAG CAG TCA AGC ACT GCC AAG TCA GGC ACC TGG ACG TAT TCC ACC GAA CTG AAG AAG
 F Q Q S S T A K S A T W T Y S T E L K K
 601/201 631/211
 CTG TAC TGC CAG ATT GCG AAG ACA TGC CCC ATC CAG ATC AAG GTG ATG ACC CCA CCC CCA
 L Y C Q I A K T C P I Q I K V M T P P P
 661/221 691/231
 CAG GGC GCT GTt ATC CGT GCC ATG CCT GTC TAC AAG AAA GCT GAG CAT GTC ACC GAG GTT
 Q G A V I R A M P V Y K K A E H V T E V
 721/241 751/251
 GTG AAA CGA TGC CCT AAC CAT GAG CTG AGC CGT GAG TTC AAT GAG GGA CAG ATT GCC CCT
 V K R C P N H E L S R E F N E G Q I A P
 781/261 811/271
 CCC AGT CAT CTG ATT CGA GTA GAA GGG AAC AGC CAT GCC CAG TAT GTA GAA GAT CCT ATC
 P S H L I R V E G N S H A Q Y V E D P I
 841/281 871/291
 ACG CGA AGG CAG AGC GTG CTG GTC CCT TAT GAG CCA CCA CAG GTT GGC ACT GAA TTC ACA
 T G R Q S V L V P Y E P P Q V G T E F T
 901/301 931/311
 ACA GTC CTG TAC aAT TTC ATG TGT AAC AGC AGC TGC GTC GGA GGA ATG AAC AGA CGT CCA
 T V L Y N F M C N S S C V G G M N R R P
 961/321 991/331
 ATT TTA ATC ATC GTT ACT CTG GAA ACC AGA GAT GGG CAA GTC CTG GGC CGA CGG TGC TTT
 I L I I V T L E T R D G Q V L G R R C F
 1021/341 1051/351
 GAG GCC CGG ATC TGT GCT TGC CCA GGA AGA GAC CGG AAG GCA GAT GAA GAC AGC ATC AGA
 E A R I C A C P G R D R K A D E D S I R
 1081/361 1111/371
 AAG CAG CAA GTA TCG GAC AGC CCA AAG AAC GGC GAT GGT AGC AAG CGC CCT TTC CGT CAG
 K Q Q V S D S A K N G D G T K R P F R Q
 1141/381 1171/391
 AAT ACA CAC CGA ATC CAG ATG ACT TCC ATC AAG AAA CGG AGA TCC CCA GAT GAT GAG CTG
 N T H G I Q M T S I K K R R S P D D E L

1201/401

CTG TAC CTA CCA GTG AGA GGT GAG ACG TAC GAG ATG TTG CTG AAG ATC GAG TCA
 L Y L P V R G R E T Y E M L L K I K E S

1261/421

CTG GAG CTC ATG CAG TAC CTC CCT CAG CAC ACG ATC GAA ACG TAC AGG CAG CAG CAG CAG
 L E L M Q Y L P Q H T I E T Y R Q Q Q Q

1321/441

CAG CAG CAC CAG CAC CTA CTT CAG AAA CAG ACC TCG ATG CAG TCT CAG TCT TCA TAT GGC
 Q Q H Q H L L Q K Q T S M Q S Q S S Y G

1381/461

AAC AGT TCC CCA CCT CTG AAC AAA ATG AAC AGC ATG AAC AAG CTG CCT TCC GTG AGC CAG
 N S S P P L N K M N S M N K L P S V S Q

1441/481

CTT ATC AAC CCA CAG CAG CGC AAT GCC CTC ACT CCC ACC ACC ATG CCT GAG GGC ATG GGA
 L I N P Q Q R N A L T P T T M P E G M G

1501/501

GCC AAC ATT CCT ATG ATG GGC ACT CAC ATG CCA ATG GCT GGA GAC ATG AAT GGA CTC AGC
 A N I P M M G T H M P M A G D M N G L S

1561/521

CCT ACC CAA GCT CTC CCT CCT CCA CTC TCC ATG CCC TCC ACC TCC CAC TGC ACC CCA CCA
 P T Q A L P P P L S M P S T S H C T P P

1621/541

CCG CCC TAC CCC ACA GAC TGC AGC ATT GTC AGG ATT tGG Caa GTC TGA
 P P Y P T D C S I V R I W Q V *

FIGURE 16 (CONT'D)

1/1 31/11
ATG AAT TTT GAA ACT TCA CGG TGT GCC ACC CTA CAG TAC TGC CCC GAC CCT TAC ATC CAG
M N F E T S R C A T L Q Y C P D P Y I Q
61/21 91/31
CGT TTC ATA GAA ACC CCA GCT CAT TTC TCG TGG AAA GAA AGT TAT TAC AGA TCT GCC ATG
R F I E T P A H F S W K E S Y Y R S A M
121/41 151/51
TCG CAG AGC ACC CAG ACA AGC GAG TTC CTC AGC CCA GAG GTC TTC CAG CAT ATC TGG GAT
S Q S T Q T S E F L S P E V F Q H J W D
181/61 211/71
TTT CTG GAA CAG CCT ATA TGC TCA GTA CAG ccc ATC GAG TTG AAC TTT GTG GAT GAA CCT
F L E Q P I C S V Q P I E L N F V D E P
241/81 271/91
TCC GAA AAT GGT GCA aca aac aag ATT GAG ATT AGC ATG GAT TGT ATC cGC ATG Caa GAc
S E N G A T N K I E I S M D C I R M Q D
301/101 331/111
TCA GAC CTC AGT GAc ccc ATG Tgg CCA CAG TAC ACG aAC cTg ggg CTC CTG aAC AGC ATg
S D L S D P M W P Q Y T N L G L L N S M
361/121 391/131
GAc cAG CAG ATT CAG AAC GGc Tcc TcG TCC ACC AGC CCC Tac aac ACA GAC CAC GCA CAG
D Q Q I Q N G S S S T S P Y N T D H A Q
421/141 451/151
AAT AGC GTG ACG GCG CCC TCG CCC TAT GCA CAG CCC AGC TCC ACC TTt GAT GCC CTC TCT
N S V T A P S P Y A Q P S S T F D A L S
481/161 511/171
CCA Tcc cct GCC ATT CCC TCC aAC ACA GAT TAC CCG GGC CCA CAC AGC TTC GAT GTG TCC
P S P A I P S N T D Y P G P H S F D V S
541/181 571/191
TTC CAG CAG TCA AGC Act GCC AAG TCA GCC Acc TGG ACG TAT TCC ACC GAA CTG AAG AAG
F Q Q S S T A K S A T W T Y S T E L K K
601/201 631/211
CTG TAC TGC CAG ATT GCG AAG ACA TGC CCC ATC CAG ATC AAG GTG ATG ACC CCA CCC CCA
L Y C Q I A K T C P I Q I K V M T P P P
661/221 691/231
CAG GGC GCT GTT ATC CGT GCC ATG CCT GTC TAC AAG AAA GCT GAG CAT GTC ACC GAG GTT
Q G A V I R A M P V Y K K A E H V T E V
721/241 751/251
GTG AAA CGA TGC CCT AAC CAT GAG CTG AGC CGT GAG TTC AAT GAG GGA CAG ATT GCC CCT
V K R C P N H E L S R E F N E G Q I A P
781/261 811/271
CCC AGT CAT CTG ATT CGA GTA GAA CGG AAC AGC CAT GCC CAG TAT GTA GAA GAT CCT ATC
P S H L I R V E G N S H A Q Y V E D P I
841/281 871/291
ACG GGA AGG CAG AGC GTG CTG GTC CCT TAT GAG CCA CCA CAG GTT GGC ACT GAA TTC ACA
T G R Q S V L V P Y E P P Q V G T E F T
901/301 931/311
ACA GTC CTG TAC AAT TTC ATG TGT AAC AGC AGC TGC GTC GGA GGA ATG AAC AGA CGT CCA
T V L Y N F M C N S S C V G G M N R R P
961/321 991/331
ATT TTA ATC ATC GTT ACT CTG GAA ACC AGA GAT GGG CAA GTC CTG GGC CGA CGG TGC TTT
I L I I V T L E T R D G Q V L G R R C F
1021/341 1051/351
GAG GCC CCG ATC TGT GCT TGC CCA GGA AGA GAC CGG AAG GCA GAT GAA GAC AGC ATC AGA
E A R I C A C P G R D R K A D E D S I R
1081/361 1111/371
AAG CAG CAA GTA TCG GAC AGC GCA AAG AAC CGC GAT GCT TTC CGT CAG AAT ACA CAC GGA
K Q Q V S D S A K N G D A F R Q N T H G
1141/381 1171/391
ATC CAG ATG ACT TCC ATC AAG AAA CGG AGA TCC CCA GAT GAT GAG CTG CTG TAC CTA CCA
I Q M T S I K K R R S P D D E L L Y L P

1201/401

GTG AGA GGT CGT GAG ACG TAC ATG TTG CTG AAG ATC AAA GAG TCA CTC CTC ATG
 V R G R E T Y M L L K I K E S L E L M

1261/421

CAG TAC CTC CCT CAG CAC ACG ATC GAA ACG TAC AGG CAG CAG CAG CAG CAC CAG
 Q Y L P Q H T I E T Y R Q Q Q Q Q Q H Q

1321/441

CAC CTA CTT CAG AAA CAT CTC CTT TCA GCC TGC TTC AGG AAT GAG CTT GTG GAG CCC CGG
 H L L Q K H L L S A C F R N E L V E P R

1381/461

GGA GAA GCT CCG ACA CAG TCT GAC GTC TTC TTT AGA CAT TCC AAC CCC CCA AAC CAC TCC
 G E A P T Q S D V F F R H S N P P N H S

1441/481

GTG TAC CCA TAG
 V Y P *

1231/411

ATG TTG CTG AAG ATC AAA GAG TCA CTC CTC CTC ATG
 V R G R E T Y M L L K I K E S L E L M

1291/431

CAG TAC CTC CCT CAG CAC ACG ATC GAA ACG TAC AGG CAG CAG CAG CAG CAC CAG
 Q Y L P Q H T I E T Y R Q Q Q Q Q Q H Q

1351/451

CAC CTA CTT CAG AAA CAT CTC CTT TCA GCC TGC TTC AGG AAT GAG CTT GTG GAG CCC CGG
 H L L Q K H L L S A C F R N E L V E P R

1411/471

GGA GAA GCT CCG ACA CAG TCT GAC GTC TTC TTT AGA CAT TCC AAC CCC CCA AAC CAC TCC
 G E A P T Q S D V F F R H S N P P N H S

FIGURE 17 (CONT'D)

1/1	31/11
ATG TTG TAC CTG gAA AAC AAT GCC CAG ACT CAA TTT AGT GAG CCA CAG TAC ACG AAC CTG M L Y L E N N A Q T Q F S E P Q Y T N L	61/21
GGG CTC CTG AAC AGC ATG GAC CAG CAG ATT CAG AAC GGC TCC TCG TCC ACC ACC CCC TAC G L L N S M D Q Q I Q N G S S S T S P Y	91/31
121/41	151/51
AAC ACA GAC CAC GCA CAG AAT AGC GTG ACG GCG CCC TCG CCC TAT GCA CAG CCC AGC TCC N T D H A Q N S V T A P S P Y A Q P S S	181/61
211/71	
ACC TTT GAT GCC CTC TCT CCA TCC CCT GCC ATT CCC TCC AAC ACA GAT TAC CCG GGC CCA T F D A L S P S P A I P S N T D Y P G P	241/81
271/91	
CAC AGC TTC GAT GTG TCC TTC CAG CAG TCA AGC ACT GCC AAG TCA GCC ACC TGG ACG TAT H S F D V S F Q Q S S T A K S A T W T Y	301/101
331/111	
TCC ACC GAA CTG AAG AAG CTG TAC TGC CAG ATT GCG AAG ACA TGC CCC ATC CAG ATC AAG S T E L K K L Y C Q I A K T C P I Q I K	361/121
391/131	
GTG ATG ACC CCA CCC CCA CAG GGC GCT GTt ATC CGT GCC ATG CCT GTC TAC AAG AAA GCT U M T P P P Q G A V I R A M P V Y K K A	421/141
451/151	
GAG CAT GTC ACC GAG GTT GTG AAA CGA TGC CCT AAC CAT GAG CTG ACC CGT GAG TTC AAT E H V T E V V K R C P N H E L S R E F N	481/161
511/171	
GAG GGA CAG ATT GCC CCT CCC AGT CAT CTG ATT CGA GTA gAA GGG AAC AGC CAT GCC CAG E G Q I A P P S H L I R V E G N S H A Q	541/181
571/191	
TAT GTA GAA GAT CCT ATC ACG GGA AGG CAG AGC GTG CTG GTC CCT TAT GAG CCA CCA CaG Y V E D P I T G R Q S V L V P Y E P P Q	601/201
631/211	
GTT GCC ACT GAA TTC ACA ACA GTC CTG TAC aAT TTC ATG TGT AAC AGC AGC TGC GTC GGA V G T E F T T V L Y N F M C N S S C V G	661/221
691/231	
GGA ATG AAC AGA CgT CCA ATT TTA ATC ATC GTT ACT CTG GAA ACC AGA GAT GGG CAA gTC G M N R R P I L I I V T L E T R D G Q V	721/241
751/251	
CTG GGC CGA CGG TGC TTT GAG GCC CGG ATC TGT GCT TGC CCA GGA AGA GAC CGG AAG GCA L G R R C F E A R I C A C P G R D R K A	781/261
811/271	
GAT GAA GAC AGC ATC AGA AAG CAG CAA GTA TCG GAC AGC GCA AAG AAC GGC GAT GGT ACG D E D S I R K Q Q V S D S A K N G D G T	841/281
871/291	
AAG CGC CCT TTC CGT CAG AAT ACA CAC GGA ATC CAG ATG ACT TCC ATC AAG AAA CGG AGA K R P F R Q N T H G I Q M T S I K K R R	901/301
931/311	
TCC CCA GAT GAT GAG CTG CTG TAC CTA CCA GTG AGA GGT CGT GAG AGC TAC GAG ATG TTG S P D D E L L Y L P V R G R E T Y E M L	961/321
991/331	
CTG AAG ATC AAA GAG TCA CTG GAG CTC ATG CAG TAC CTC CCT CAG CAC AGC ATC GAA AGC L K I K E S L E L M Q Y L P Q H T I E T	1021/341
1051/351	
TAC AGG CAG CAG CAG CAG CAG CAC CAG CAC CTA CTT CAG AAA CAG ACC TCG ATG CAG Y R Q Q Q Q Q Q H Q H L L Q X Q T S M Q	1081/361
1111/371	
TCT CAG TCT TCA TAT GGC AAC AGT TCC CCA CCT CTG AAC AAA ATG AAC ACC ATG AAC AAG S Q S S Y G N S S P P L N K M N S M N K	1141/381
1171/391	
CTG CCT TCC GTG AGC CAG CTT ATC AAC CCA CAG CAG CGC AAT GCC CTC ACT CCC ACC ACC L P S V S Q L I N P Q Q R N A L T P T T	

1201/401 1231/411
 ATG CCT GAG GGC ATG GGA GCC AAC ATT CCT ATG ATG GGC ACT CAC ATG CCA ATG GCT GGA
 M P E G M G A N I P M M G T H M P M A G
 1261/421 1291/431
 GAC ATG AAT CGA CTC AGC CCT ACC CAA GCT CTC CCT CCT CCA CTC TCC ATG CCC TCC ACC
 D M N G L S P T Q A L P P P L S M P S T
 1321/441 1351/451
 TCC CAC TGC ACC CCA CCA CCG CCC TAC CCC ACA GAC TGC AGC ATT GTC AGT TTC TTA GCA
 S H C T P P P Y P T D C S I V S F L A
 1381/461 1411/471
 Agg Ttc ggC TGC TCA TCA TGC CTG GAC TAT TTC ACG ACC CAG ggg CTG Acc ACC ATC TaT
 R L G C S S C L D Y F T T Q G L T T I Y
 1441/481 1471/491
 CAG ATT GAG CAT TAC TCC ATG GAT GAT Ttg GCa aGT CTG AAG ATc ccT GAA CAG TTC CGA
 Q I E K Y S M D D L A S L K I P E Q F R
 1501/501 1531/511
 CAT GCC ATC TGG AAg GGC aTC CTG GAc CAC AGG cAG CTG CAC GAC TTC TCC TCA CCT CCT
 H A I W K G I L D H R Q L H D F S S P P
 1561/521 1591/531
 CaT CTC CTG AGG ACC CCA AGT CGT GCC TCT ACC GTC AGT GTG GGC TCC AGT GAG ACC CGT
 H L L R T P S G A S T V S V G S S E T R
 1621/541 1651/551
 GGT GAA CGT GTG ATC GAT GCC GTG CGC TTT ACC CTC CGC CAG ACC ATC TCT TTT CCA CCC
 G E R V I D A V R F T L R Q T I S F P P
 1681/561 1711/571
 CGT GAC GAG TGG AAT GAT TTC AAC TTT GAC ATG GAT TCT CGT CGC AAC AAG CAG CAG CGT
 R D E W N D F N F D M D S R R N K Q Q R
 1741/581
 aTC AAA GAG GAA GGA GAA TGA
 I K E E G E *

1/1 31/11
 ATG TTG TAC CTG GAA AAC AAT GCC CAG ACT CAA TTT AGT GAG CCA CAG TAC ACG AAC CTG
 M L Y L E N N A Q T Q F S E P Q Y T N L
 61/21 91/31
 GGG CTC CTG AAC AGC ATG GAC CAG CAG ATT CAG AAC GGC TCC TCG TCC ACC AGC CCC TAC
 G L L N S M D Q Q I Q N G S S S T S P Y
 121/41 151/51
 AaC ACA GAC CAC GCA CAG AAT AGC GTG ACG GCG CCC TCG CCC TAT GCA CAG CCC AGC TCC
 N T D H A Q N S V T A P S P Y A Q P S S
 181/61 211/71
 ACC TTT GAT GCC CTC TCT CCA TCC CCT GCC ATT CCC TCC AAC ACA GAT TAC CCG GGC CCA
 T F D A L S P S P A I P S N T D Y P G P
 241/81 271/91
 CAC AGC TTC GAT GTG TCC TTC CAG CAG TCA AGC ACT GCC AAG TCA GCC ACC TGG ACG TAT
 H S F D V S F Q Q S S T A K S A T W T Y
 301/101 331/111
 TCC ACC GAA CTG AAG AAG CTG TAC TGC CAG ATT GCG AAG ACA TGC CCC ATC CAG ATC AAG
 S T E L K K L Y C Q I A K T C P I Q I K
 361/121 391/131
 GTG ATG ACC CCA CCC CCA CAG GGC GCT GTT ATC CGT GCC ATG CCT GTC TAC AAG AAA GCT
 V M T P P P Q G A V I R A M P V Y K K A
 421/141 451/151
 GAG CAT GTC ACC GAG GTT GTG AAA CGA TGC CCT AAC CAT GAG CTG AGC CGT GAG TTC AAT
 E H V T E V V K R C P N H E L S R E F N
 481/161 511/171
 GAG GGA CAG ATT GCC CCT CCC AGT CAT CTG ATT CGA GTA gAA GGG AAC AGC CAT GCC CAG
 E G Q I A P P S H L I R V E G N S H A Q
 541/181 571/191
 TAT GTA GAA GAT CCT ATC ACG GGA AGG CAG AGC GTG CTG GTC CCT TAT GAG CCA CCA CAG
 Y V E D P I T G R Q S V L V P Y E P P Q
 601/201 631/211
 GTT GGC ACT GAA TTC ACA ACA GTC CTG TAC aAT TTC ATG TGT AAC AGC AGC TGC GTC GGA
 V G T E F T T V L Y N F M C N S S C V G
 661/221 691/231
 GGA ATG AAC AGA CGT CCA ATT TTA ATC ATC GTT ACT CTG GAA ACC AGA GAT CGG CAA gTC
 G M N R R P I L I I V T L E T R D G Q V
 721/241 751/251
 CTG GGC CGA CGG TGC TTT GAG GCC CGG ATC TGT GCT TGC CCA GGA AGA GAC CGG AAG GCA
 L G R R C F E A R I C A C P G R D R K A
 781/261 811/271
 GAT GAA GAC AGC ATC AGA AAG CAG CAA GTA TCG GAC AGC GCA AAG AAC GGC GAT GGT ACG
 D E D S I R K Q Q V S D S A K N G D G T
 841/281 871/291
 AAG CGC CCT TTC CGT CAG AAT ACA CAC GGA ATC CAG ATG ACT TCC ATC AAG AAA CGG AGA
 K R P F R Q N T H G I Q M T S I K K R R
 901/301 931/311
 TCC CCA GAT GAT GAG CTG CTG TAC CTA CCA GTG AGA GGT CGT GAG AGC TAC GAG ATG TTG
 S P D D E L L Y L P V R G R E T Y E M L
 961/321 991/331
 CTG AAG ATC AAA GAG TCA CTG GAG CTC ATG CAG TAC CTC CCT CAG CAC ACG ATC GAA ACG
 L K I X E S L E L M Q Y L P Q H T I E T
 1021/341 1051/351
 TAC AGG CAG CAG CAG CAG CAG CAC CAG CAC CTA CTT CAG AAA CAG ACC TCG ATG CAG
 Y R Q Q Q Q Q H Q H L L Q K Q T S M Q
 1081/361 1111/371
 TCT CAG TCT TCA TAT GGC AAC AGT TCC CCA CCT CTG AAC AAA ATG AAC AGC ATG AAC AAG
 S Q S S Y G N S S P P L N K M N S M N K
 1141/381 1171/391
 CTG CCT TCC GTG AGC CAG CTT ATC AAC CCA CAG CAG CGC AAT GCC CTC ACT CCC ACC ACC
 L P S V S Q L I N P Q Q R N A L T P T T

FIGURE 19

1201/401

ATG CCT GAG GGC ATG GGA GCC A ATT CCT ATG ATG GGC ACT CAC ATG CCA A GCT GGA
 M P E G M G A N I P M M G T H M P M A G

1261/421

1291/431
 GAC ATG AAT GGA CTC ACC CCT ACC CAA GCT CTC CCT CCA CTC TCC ATG CCC TCC ACC
 D M N G L S P T Q A L P P L S M P S T

1321/441

1351/451
 TCC CAC TGC ACC CCA CCA CCG CCC TAC CCC ACA GAC TGC AGC ATT GTC AGG ATT tGG Caa
 S H C T P P P Y P T D C S I V R I W Q

1381/461

GTC TGA

V *

DRAFT - DO NOT DISTRIBUTE

FIGURE 19 (CONT'D)

1/1 31/11
ATG TTG TAC CTG GAA AAC AAT GCC CAG ACT CAA TTT AGT GAG CCA CAG TAC ACG AAC CTG
M L Y L E N N A Q T Q F S E P Q Y T N L
61/21 91/31
GGG CTC CTG AAC AGC ATG GAC CAG CAG ATT CAG AAC GGC TCC TCG TCC ACC ACC CCC TAC
G L L N S M D Q Q I Q N G S S S T S P Y
121/41 151/51
AAC ACA GAC CAC GCA CAG AAT AGC GTG ACG GCG CCC TCG CCC TAT GCA CAG CCC AGC TCC
N T D H A Q N S V T A P S P Y A Q P S S
181/61 211/71
ACC TTT GAT GCC CTC TCT CCA TCC CCT GCC ATT CCC TCC AAC ACA GAT TAC CCG GGC CCA
T F D A L S P S P A I P S N T D Y P G P
241/81 271/91
CAC AGC TTC GAT GTG TCC TTC CAG CAG TCA AGC ACT GCC AAG TCA GCC ACC TGg ACG TAT
H S F D V S F Q Q S S T A K S A T W T Y
301/101 331/111
TCC ACC GAA CTG AAG AAG CTG TAC TCC CAG ATT GCG AAG ACA TGC CCC ATC CAG ATC AAG
S T E L K K L Y C Q I A K T C P I Q I K
361/121 391/131
GTG ATG ACC CCA CCC CCA CAG GGC GCT GTT ATC CGT GCC ATG CCT GTC TAC PAG AAA GCT
V M T P P P Q G A V I R A M P V Y K K A
421/141 451/151
GAG CAT GTC ACC GAG GTT GTG AAA CGA tGC CCT AAC CAT GAG CTG AGC CGT GAG TTC AAT
E H V T E V V K R C P N H E L S R E F N
481/161 511/171
GAG GGA CAG ATT GCC CCT CCC AGT CAT CTG ATT CGA GTA GAA GGG AAC AGC CAT GCC CAG
E G Q I A P P S H L I R V E G N S H A Q
541/181 571/191
TaT GTA GAA gAT CCT ATC aCG GGA AGG CAG AGC GTG CTG GTC CCT tAT GAG CCA CCA CAG
Y V E D P I T G R Q S V L V P Y E P P Q
601/201 631/211
GTT GGC ACT GAA TTC ACA ACA gTC CTG TAC AAT TTC ATG TGT aAC AGC AGC TGC GTC GGA
V G T E F T T V L Y N F M C N S S C V G
661/221 691/231
GGA ATG AAC AGA CGT CCA aTT TTA ATC ATC GTT ACT CTG GAA ACC AgA GAT GGG CAA GTC
G M N R R P I L I I V T L E T R D G Q V
721/241 751/251
CTG GGC CGA CGG TGC TTT GAG GCC CGG ATC TGT GCT TGC CCA GGA AGA GAC CGG AAG GCA
L G R R C F E A R I C A C P G R D R K A
781/261 811/271
GAT GAA GAC AGC ATC AGA AAG CAG CAA GTA TCG GAC AGC GCA AAG AAC GGC GAT GCT TTC
D E D S I R K Q Q V S D S A K N G D A F
841/281 871/291
CGT CAG AAT ACA CAC GGA ATC CAG ATG ACT TCC ATC AAG AAA CGG AGA TCC CCA GAT GAT
R Q N T H G I Q M T S I K K R R S P D D
901/301 931/311
GAG CTG CTG TAC CTA CCA GTG AGA GGT CGT GAG AGC TAC GAG ATG TTG CTG AAG ATC AAA
E L L Y L P V R G R E T Y E M L L K I K
961/321 991/331
GAG TCA CTG GAG CTC ATG CAG TAC CTC CCT CAG CAC ACG ATC GAA AGC TAC AGG CAG CAG
E S L E L M Q Y L P Q H T I E T Y R Q Q
1021/341 1051/351
CAG CAG CAG CAG CAC CAC CTA CTT CAG AAA CAT CTC CTT TCA GCC TGC TTC AGG AAT
Q Q Q Q H Q H L L Q K H L L S A C F R N
1081/361 1111/371
GAG CTT GTG GAG CCC CGG GCA GAA GCT CCG ACA CAG TCT GAC GTC TTC TTT AGA CAT TCC
E L V E P R G E A P T Q S D V F F R H S
1141/381
AAC CCC CCA AAC CAC TCC GTG TAC CCA TAG
N P P N H S V Y P *

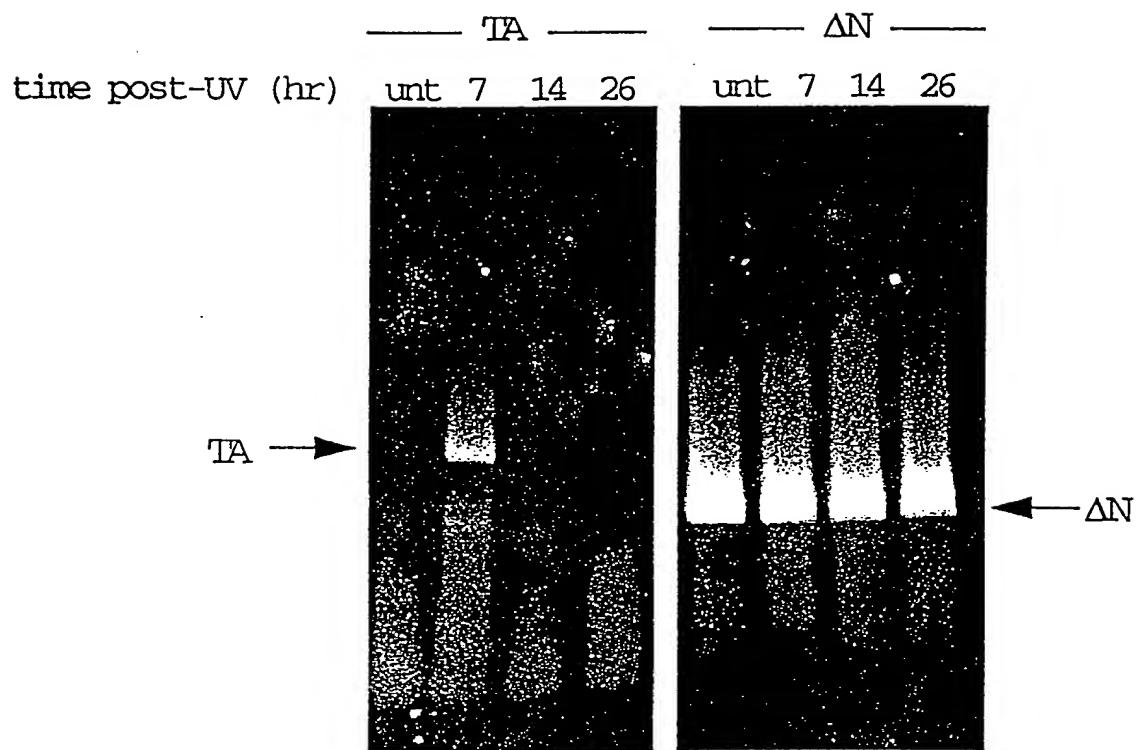


Figure 21. UV Induction of TA-p63 transcript. Primary human foreskin keratinocytes were exposed to UV irradiation (300J/m^2), then harvested at times indicated. Total RNA was prepared, and RT-PCR on equal amounts of RNA was performed using primers specific for transactivating (TA) or truncated (ΔN) N-terminal domains of p63 (Yang et al., 1998). TA-p63 is not detectable in untreated (unt) keratinocytes, but expression is induced at 7hrs after UV treatment. ΔN -p63 appears to remain unchanged from untreated cells at all time points taken.

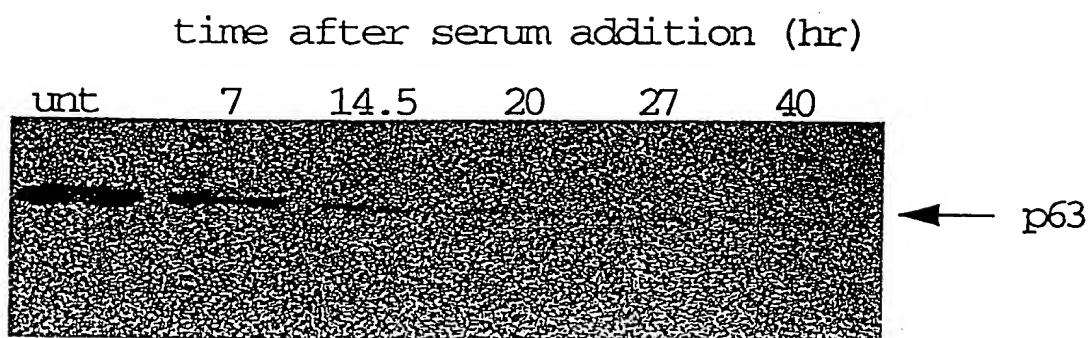


Figure 22. p63 protein expression decreases upon keratinocyte differentiation.
Primary human foreskin keratinocytes were treated with 10% fetal bovine serum to induce differentiation, and harvested at times indicated. Cells were lysed in RIPA buffer, boiled in Lammeli buffer, and proteins fractionated by SDS gel electrophoresis. Immunoblotting was performed using an anti-p63 mouse monoclonal antibody, 4A4, which recognizes all p63 isoforms identified to date. p63 protein levels in keratinocytes are seen to decrease progressively upon differentiation, as compared to untreated (unt) samples.

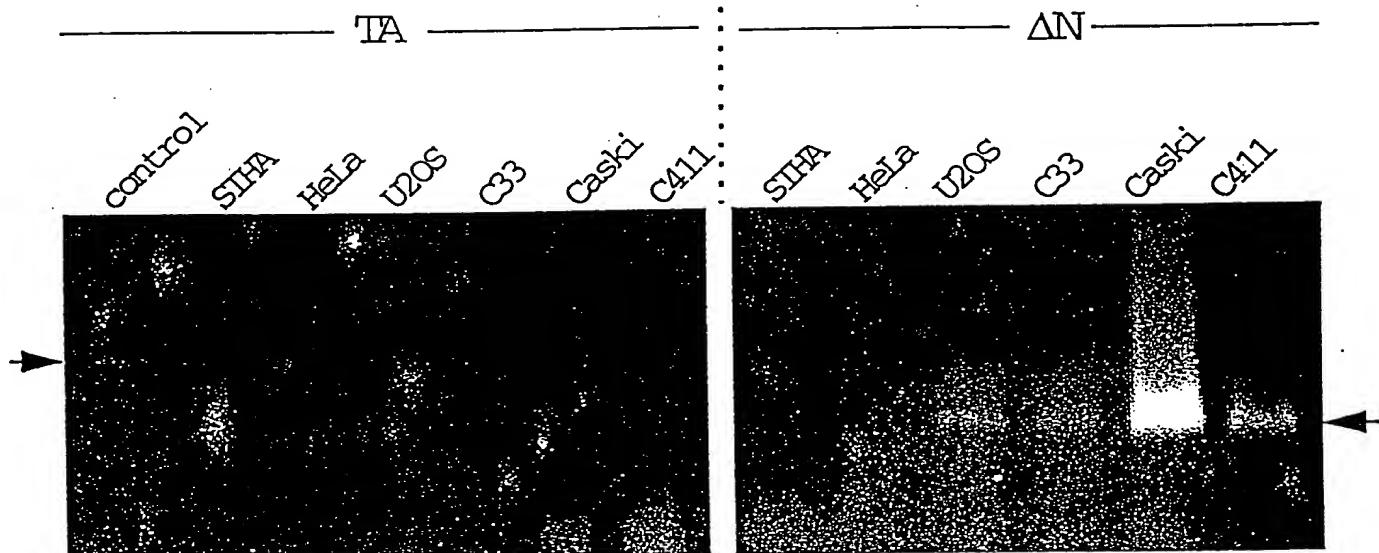


Figure 23. p63 RNA expression in human cancer cell lines. RT-PCR was performed on total RNA from several human tumor cell lines* using primers specific for transactivating (TA) or truncated (Δ N) N-terminal domains of p63 (see Figure 1), as indicated. Amongst these cell lines, only the ME180 control cell line showed a TA-p63 transcript. Instead, a majority showed expression of Δ N-p63, which has been demonstrated to act as a dominant negative protein towards both the tumor suppressor p53, as well as transactivating isoforms of p63.

*note: all are cervical carcinoma cell lines except U2OS, which is a human osteocarcinoma line.

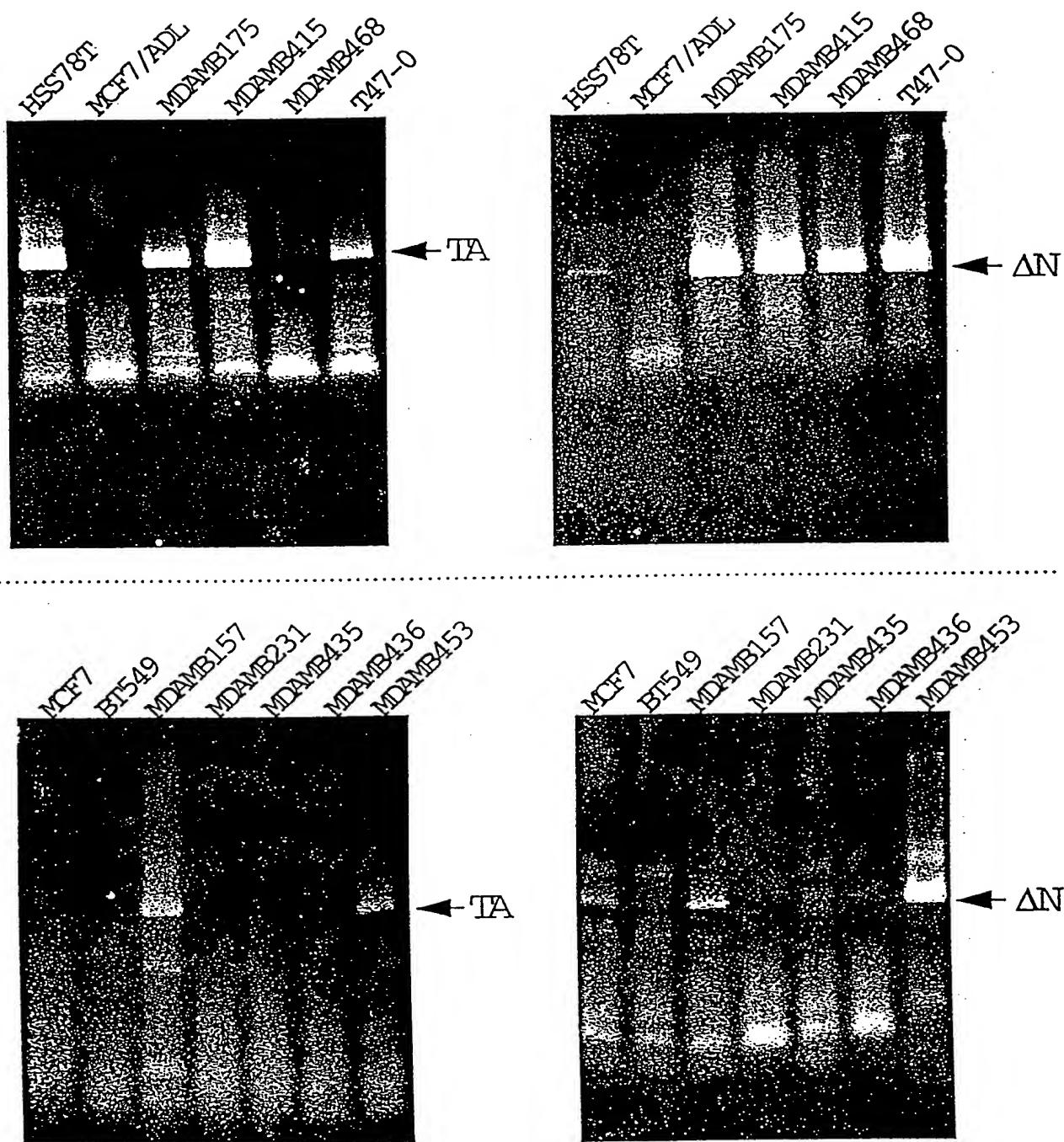
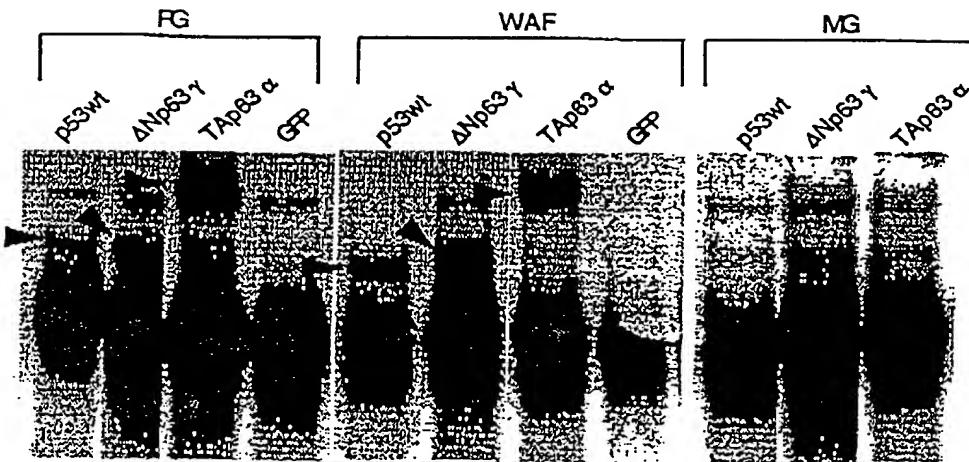


Figure 24. p63 RNA expression in human breast cancer cell lines. RT-PCR was performed on total RNA from breast cancer cell lines using primers specific for transactivating (TA) or truncated (Δ N) N-terminal domains of p63 (see Figure 1), as indicated. p63 was detected in a majority of cell lines tested, with some specimens containing both transcript isotypes.



Electrophoretic mobility shift assays (EMSA) were performed using three separate, ^{32}P radiolabeled oligonucleotides: a minimal p53 binding sequence site (PG), a p53 binding site in the p21 promoter (WAF), and a mutant p53 binding site (MG, *Kern et al., 1992) with lysates of 293 human kidney cells transfected with p53, $\Delta\text{Np63}\gamma$, TAp63 α , and green fluorescent protein (GFP). p53, $\Delta\text{Np63}\gamma$, and TAp63 α lysates all yielded significant mobility shifts of both PG and WAF oligonucleotides (highlighted by arrows), while the GFP protein, included as negative control, failed to display a similar shift. None of the lysates showed a shift of the control, non-p53 binding oligonucleotide, MG, thus demonstrating the specificity of p53, $\Delta\text{Np63}\gamma$, and TAp63 α interactions with the p53-binding sites.

FIGURE 25

Relative Efficiency Plot TA and Delta

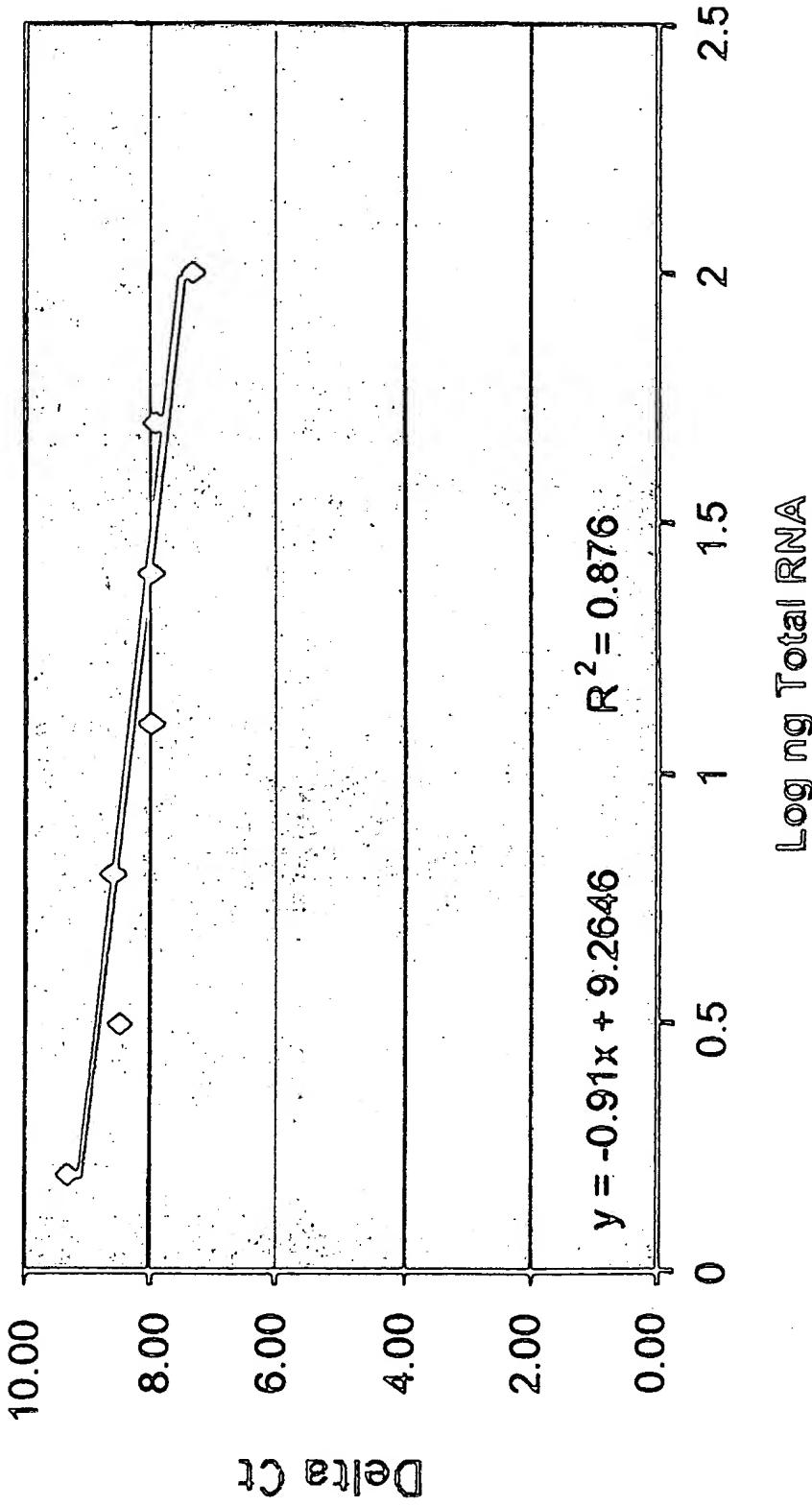


FIGURE 26

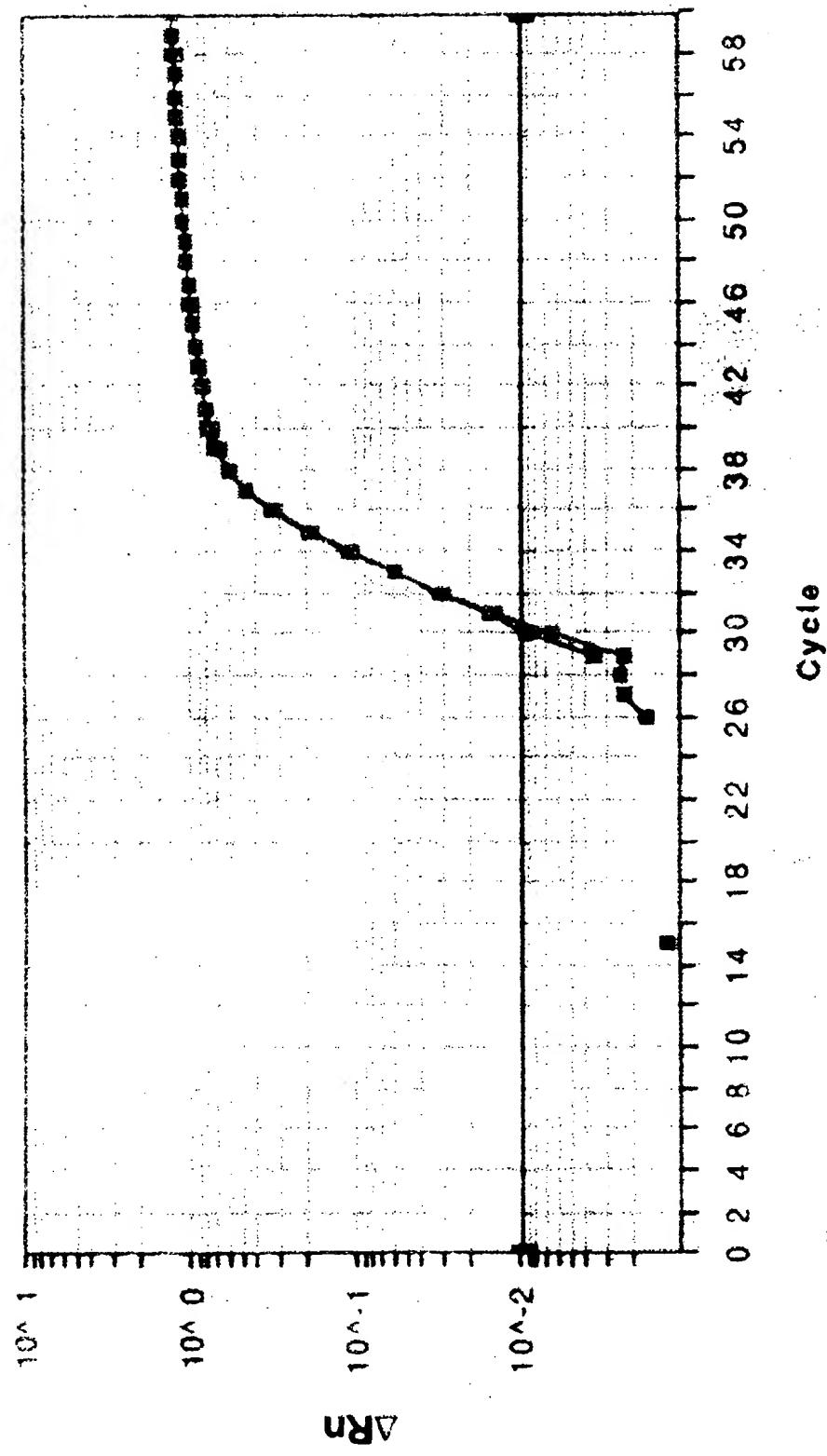
A. TAp63 amplification plot for PrEC cells

FIGURE 27(A)

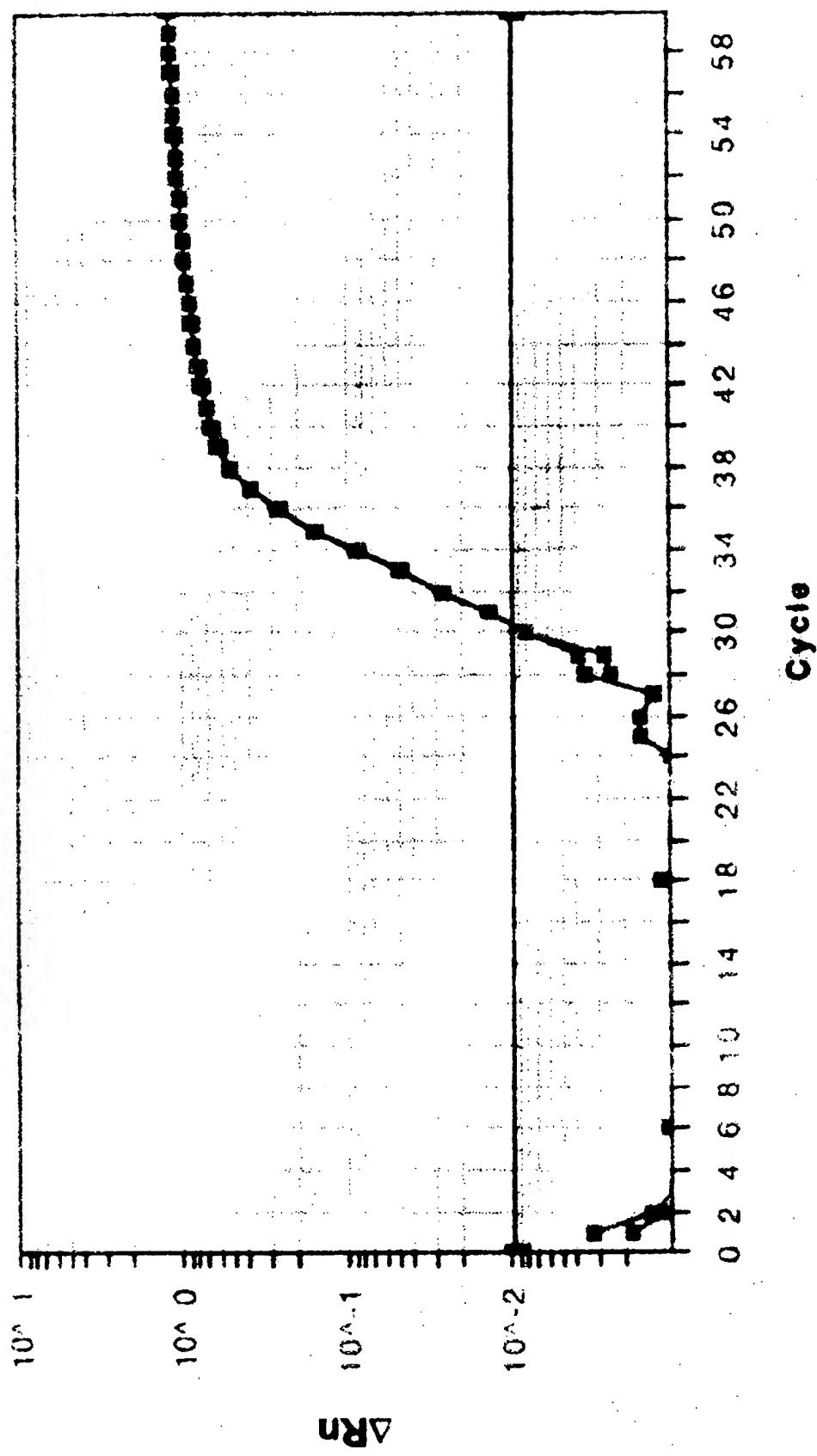
B. TAp63 amplification plot for PC3 cells

FIGURE 27 (B)

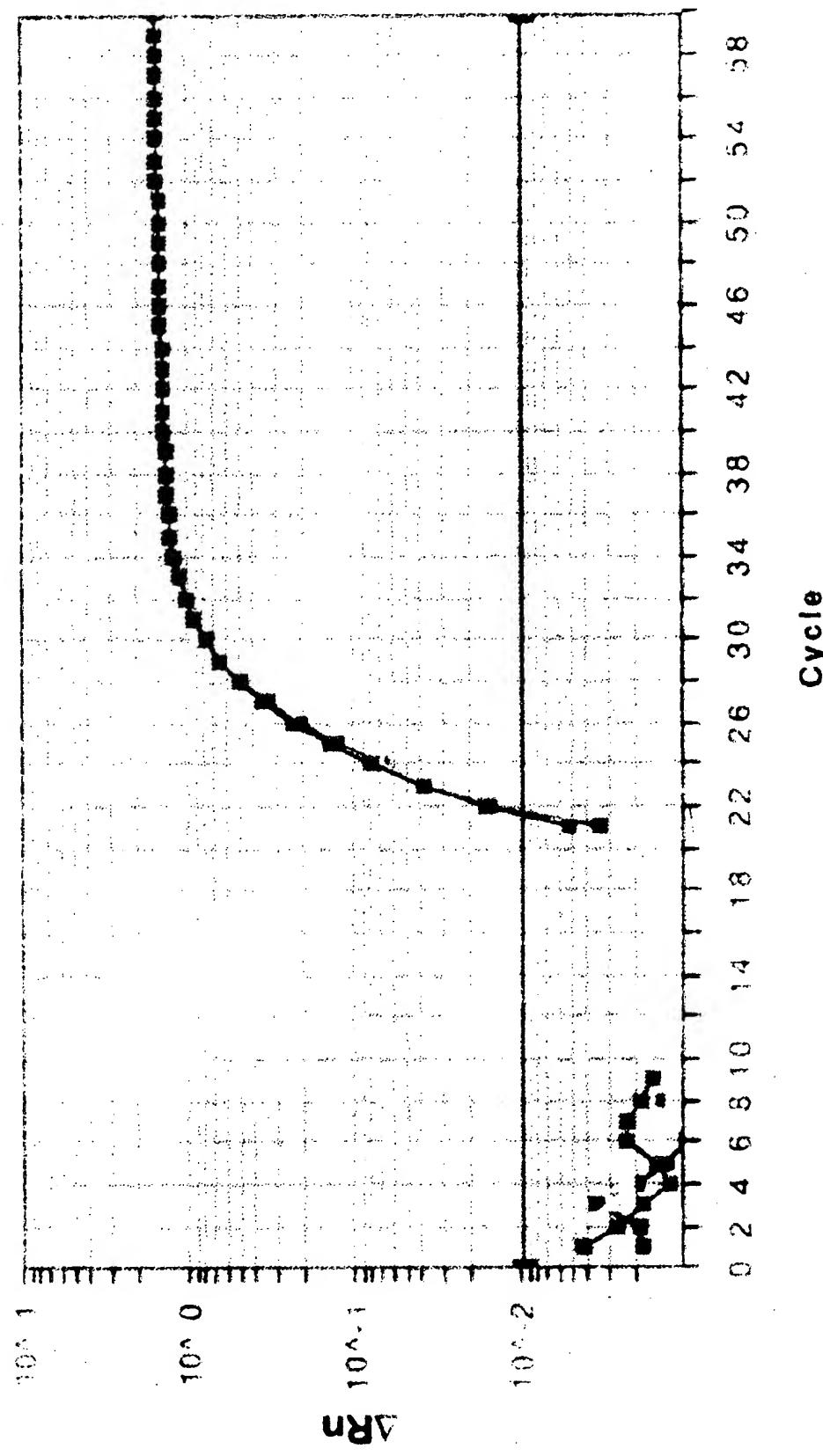
C. ΔNP63 amplification plot for PrEC cells

FIGURE 27 (C)

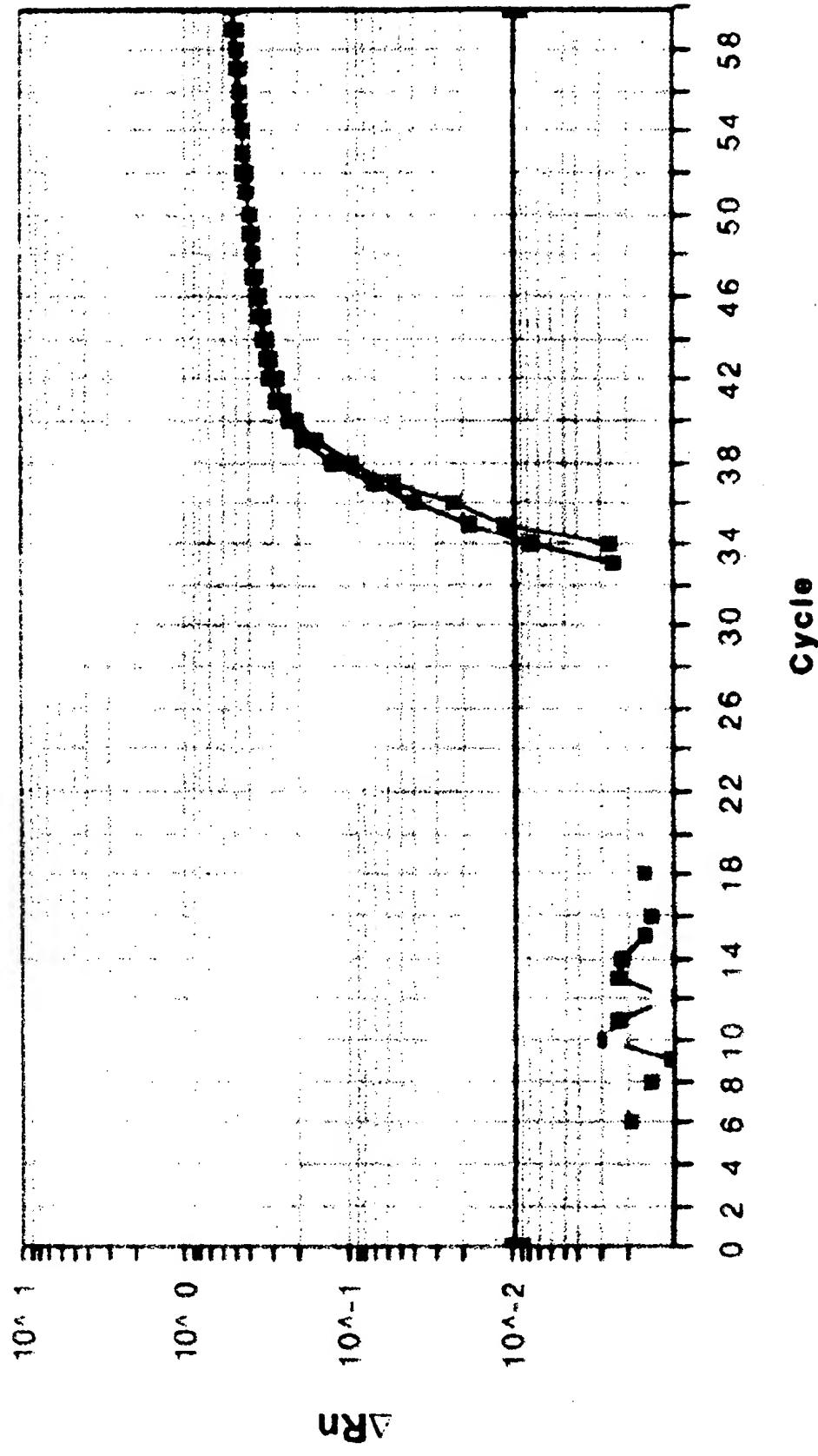
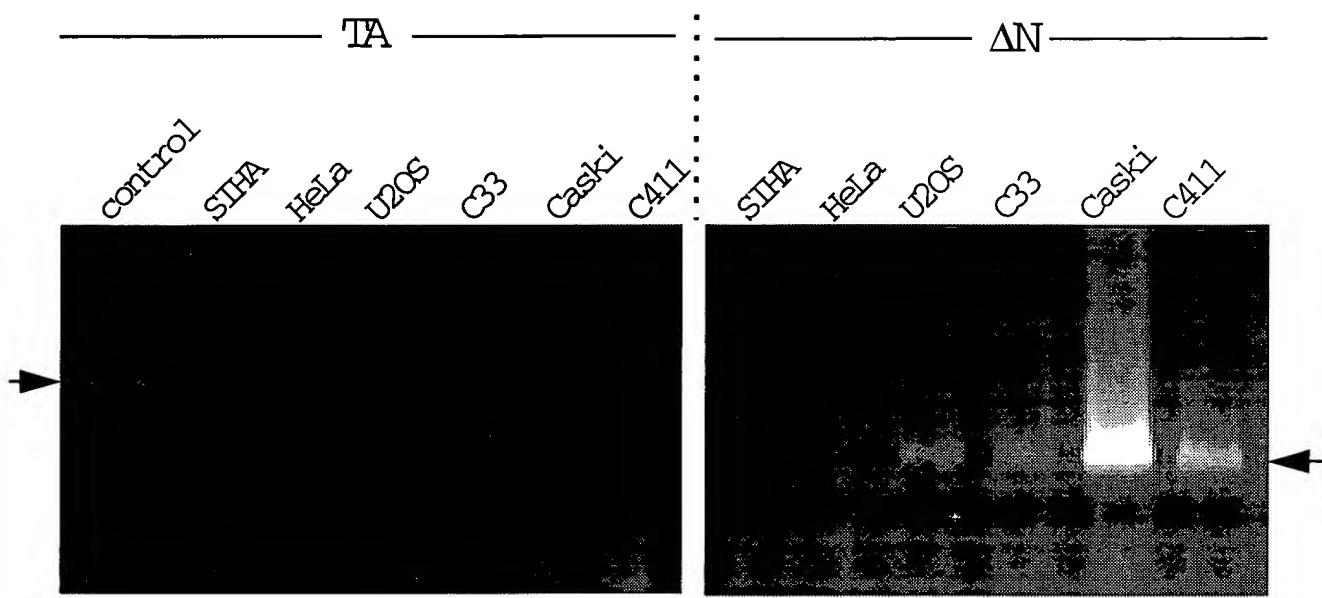
D. $\Delta Np63$ amplification plot for PC3 cells

FIGURE 27(D)



p63 RNA expression in human cancer cell lines. RT-PCR was performed on total RNA from several human tumor cell lines* using primers specific for transactivating (TA) or truncated (Δ N) N-terminal domains of p63, as indicated. Amongst these cell lines, only the ME180 control cell line showed a TA-p63 transcript. Instead, a majority showed expression of Δ N-p63, which has been demonstrated to act as a dominant negative protein towards both the tumor suppressor p53, as well as transactivating isoforms of p63.

*note: all are cervical carcinoma cell lines except U2OS, which is a human osteocarcinoma line.

FIGURE 28

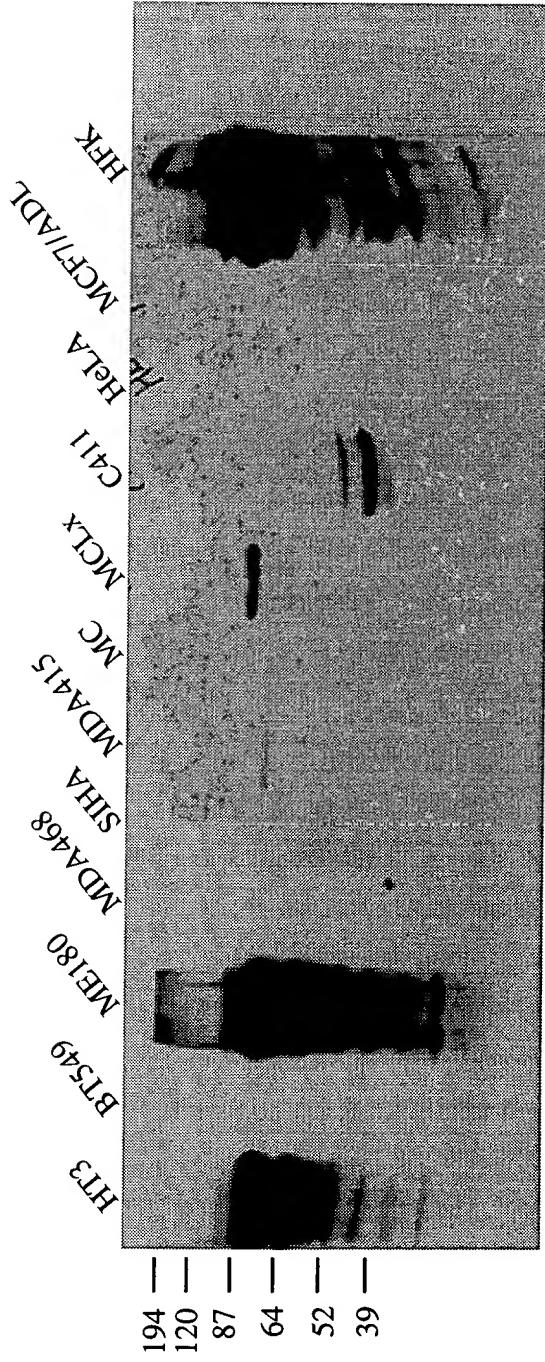
4A4 anti-p63

FIGURE 29